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Review article

Effects of altrenogest on reproductive performance of gilts and sows: A meta-analysis

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ABSTRACT

Altrenogest is a synthetic progestogen that allows for synchronization of the time of estrus in swine. Its effect on reproductive performance, however, is inconsistent due to conflicting data in the scientific literature. A meta-analysis of published data, therefore, was performed to determine whether altrenogest affects gilt and sow reproductive performance. Altrenogest administration to pigs enhanced the number of piglets born alive per litter (NBA), total number born per litter (TNB), estrous rate within 10 days after treatment (ER_{10}) and pregnancy rate (PR) as well as the farrowing rate (FR) of gilts. The NBA and TNB of primiparous sows fed altrenogest were improved although FR was less. In multiparous sows, altrenogest treatment did not result in any improvement for any of the five analyzed variables. Additionally, 14-day treatment regimens for gilts and > 8-days for primiparous sows improved reproductive performance and extent of estrous synchrony. The effects of altrenogest on reproductive performance of swine were parity and treatment duration dependent.

1. Introduction

Altrenogest (allyltrenbolone, 17a-allyl-17b-hydroxy-estra-4,9,11-trien-3-one) is a synthetic progestogen that suppresses ovarian follicular development. Its primary use is for estrous synchronization in gilts and primiparous sows (Kraeling and Webel, 2015; Lopes et al., 2017). Altrenogest is used for the precise synchronization of time of estrus at rates up to 93% during 4 to 7 days post administration (Martinat-Botté et al., 1995; Fernandez et al., 2005). Although in numerous studies there have been attempts to use altrenogest to improve subsequent reproduction of gilts and sows, there is no clear consensus on the benefits of such treatments. For example, Martinat-Botté et al. (1990; 1995; 2010) reported that gilts or sows treated with altrenogest had greater farrowing (88.4% > 80.8%, $P < 0.05$), estrous (83.4% > 79.6%, $P < 0.05$) and pregnancy rates (89.3% > 77.4%, $P < 0.05$) as well as a larger litter size (9.6 > 9.1, $P < 0.05$). Nevertheless, in other studies (e.g., Fernandez et al., 2005; van Leeuwen et al., 2011a) altrenogest treatment had no positive effect and even a negative effect on these reproductive variables. The inconsistency in these findings might have resulted from small sample sizes or the experimental conditions. Hence, it is necessary to make a systematic and quantitative assessment of published studies for a comprehensive conclusion.

Over the past few years, meta-analysis, an important method for synthesis of data from previously conducted research, has become increasingly popular in fields as diverse as medicine, pharmacy, psychology and the social sciences (Böhning et al., 2003; Bax et al., 2006). This type of analysis has also been used for evaluation of treatment effects in animal science and veterinary medicine. For example, Chen et al. (2011) investigated the effects of biotin on milk performance of dairy cattle using a meta-analysis. Duffield

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et al. (2008) performed a meta-analysis to ascertain the effect of monensin on metabolism of dairy cattle; and Yan et al. (2016) assessed efficacy of progesterone supplementation during early pregnancy in cows by a meta-analysis. A well-conducted meta-analysis provides an unbiased overview of available studies.

Considering the widespread use of altrenogest in pigs and inconsistency of results among studies, a meta-analysis might be helpful in elucidating effects of altrenogest on subsequent reproduction of pigs after there has been altrenogest treatments and provide insights as to why there have been inconsistent results among previous studies. In this manuscript, the aim was to evaluate the efficacy of altrenogest for improving estrous rate within 10 days after treatment (ER_{10}), pregnancy rate (PR), farrowing rate (FR), number of pigs born alive per litter (NBA) and total number of pigs born per litter (TNB) of gilts and sows, by performing a meta-analysis of data from all available studies where there was altrenogest administered.

2. Materials and methods

2.1. Search strategy and selection criteria

A comprehensive and systematic search of English literature in Science Direct, Web of Science, PubMed, Ovid, EMA website and Google Scholar was performed. The keywords used for searching were as follows: “altrenogest and swine”, “altrenogest and pig”, “altrenogest and gilt”, “altrenogest and sow”, “allyltrenbolone and swine”, “allyltrenbolone and pig”, “allyltrenbolone and gilt”, and “allyltrenbolone and sow”. Furthermore, citations in the retrieved articles were reviewed to search for additional relevant studies.

Studies were included if (1) these were designed as a randomized controlled trial (RCT) or a clinically controlled trial (CCT); (2) the population studied was gilts or sows; (3) the dosage of altrenogest was 15–30 mg/d; and (4) all data except for NBA and TBA data were expressed as either Mean ± SD (standard deviation) or Mean ± SE (standard error). Studies that were not published as full reports were excluded and conference papers were crosschecked with journal papers to avoid repetition of data.

2.2. Data extraction

Data were extracted independently by two investigators (Z. Wang and L.Q. Wang) and assessed by the other authors. Discrepancies were resolved by consensus. A template for data extraction including mean, standard deviation, and number of pigs in each group was drafted. The following data were abstracted from included studies: year, country, number of trails, type of swine, dose of altrenogest, duration of treatment, number of trial sites, number of animals, breed and reproductive variables including ER_{10}, PR, FR, NBA, and TNB (Table 1). Weaning-to-estrous interval (WEI) and birth weight (BW) were not analyzed for WEI was calculated by different intervals in different studies and relevant data for BW were insufficient for meta-analysis. Precision of estimate was based on the SD values of treated and control groups reported in the publications. If only a SE was provided, SD was calculated by multiplying the SE of means by the square root of the number of pigs.

2.3. Statistical analysis

A meta-analysis was performed on the extracted data using Stata software (Intercooled Stata V. 12.0; Stata Corp, College Station, TX, USA). For continuous outcomes, a weighted mean difference (WMD) with 95% confidence interval (95% CI) was calculated. For dichotomous outcomes, an odds ratio (OR) with 95% confidence interval was calculated. Each study was weighted on the basis of the inverse of the variance. Statistical significance was considered at $P < 0.05$. *A priori* subgroup analyses were conducted based on parity and treatment duration.

Heterogeneity among studies was assessed using I^2-statistic and a guide for interpretation of I^2 was as follows: 0%–25%, no heterogeneity; 25%–50%, low heterogeneity; 50%–75%, moderate heterogeneity; 75%–100%, high heterogeneity (Higgins et al., 2003). A fixed effects model was used if studies were homogeneous and a random effect model was utilized if studies were heterogeneous. Forest plots were created to depict means and the confidence intervals in a graphic manner. The WMD in NBA and TNB; and OR in ER_{10}, PR and FR between altrenogest-treated and control group was the outcome of interest listed in the forest plots. Begg’s test and funnel plots were used to investigate the publication bias (Begg and Mazumdar, 1994; Sterne and Egger, 2001). The *P*-values < 0.05 were considered statistically significant for publication bias.

3. Results

3.1. Identification of studies

There were 358 articles identified from the search of published literature. Only 26 studies met inclusion criteria and this set was used for meta-analysis. These included studies were from the United States, France, Argentina, Australia, Brazil, New Zealand, Japan, Canada, Thailand, Ireland, Belgium and Spain (Table 1). Because one study (FDA, 2003) was conducted in the United States and Canada, 27 locations were included.

3.2. Meta-analysis

Pooled estimations were used to identify effects of altrenogest on gilt and sow reproductive performance. The NBA (WMD = 0.55,