SYNCHRONIZATION OF ESTRUS IN SWINE WITH ALLYL TRENbolONE (RU-2267)

Robert R. Kraeling1, Phillip J. Dziuk2, Vernon G. Pursel3, George B. Rampacek4 and Stephen K. Webel5,6

Summary

Studies were conducted in Georgia, Illinois and Maryland, representing three geographical regions of the United States, to determine the dose range of the orally active progestin, allyl trenbolone (RU-2267), for effective synchronization of estrus in swine. Animals that had displayed estrus at least once were group-fed for 18 days 5, 10, 20 or 40 mg of RU-2267 incorporated into a daily diet of 1.8 or 2.3 kg of feed. The numbers of gilts given each respective dose were eight, eight, eight and seven in Georgia, and six, five, six and six in Illinois. Five pigs received each dose in Maryland. Five primiparous sows were also treated with each dose in Maryland. Estrus was checked daily with a boar, and ovaries were examined by laparotomy 4 to 10 days after the estrous period following treatment or 15 to 24 days after the end of treatment in those animals that failed to display estrus. In Maryland, the interval from end of treatment to estrus (interval to estrus) differed (P<.05) between gilts (5.4 ± .3) and sows (6.0 ± .2) fed the 20-mg dose; but no other age differences were detected, and, as a result, data for gilts and sows were combined. The percentage of animals displaying a post-treatment estrus (estrous response) and the average number of corpora lutea (CL) formed at the post-treatment estrus (ovulation rate) were similar at the three locations; however, interval to estrus was shorter (P<.05) and the percentage of animals with follicular and(or) luteal cysts (percentage cystic) was lower (P<.05) in Illinois than in Georgia or Maryland. Estrous response, interval to estrus, percentage cystic and ovulation rate at the four doses of RU-2267 were, respectively: 5 mg—67%, 4.6 ± .2 days, 58% and 13.4 ± 1.3; 10 mg—82%, 4.3 ± .2, 22% and 16.4 ± .9; 20 mg—100%, 5.6 ± .2 days, 0% and 15.0 ± .8; 40 mg—100%, 6.1 ± .2 days, 0% and 14.7 ± .8. These results show that the most effective doses of RU-2267 for synchronizing estrus and ovulation without inducing development of follicular and(or) luteal cysts were 20 and 40 mg and that the minimum effective dose of RU-2267 for synchronizing estrus was between 10 and 20 milligrams.

(Key Words: Progestin, Swine, Ovulation, Synchronization of Estrus.)

Introduction

An effective method of controlling the time of estrus and ovulation in swine has been sought by researchers for the past 30 years. Webel (1978) recently reviewed the literature on ovulation control in swine. The primary approaches have involved treatments that suppressed release of pituitary gonadotropins for 15 to 20 days and thereby inhibited follicle growth and subsequent ovulation. Corpora lutea (CL) regressed spontaneously during the period of pituitary suppression, and, after cessation of treatment, resumption of gonadotropin secretion stimulated follicular growth and ovulation. Progesterone (Ulberg et al., 1951; Baker et al., 1954) and some orally active synthetic progestins (Baker et al., 1954; Dziuk, 1960 and 1964; Nellor, 1960; Nellor et al., 1961; Wagner and Seerley, 1961; Dziuk and Baker, 1962; First et al., 1963; Dziuk and Polge, 1965; Pond et al., 1965; Veenhuizen et

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al., 1965; Ray and Seerley, 1966) were most commonly used. In general, these compounds were not totally effective, because the post-treatment estrus was often accompanied by development of cystic ovaries, decreased fertility and(or) imprecise synchronization of estrus and ovulation.

Newer orally active progestins have been effective and practical for use in controlling estrus and ovulation in swine (Mayer and Schütze, 1977; Schütze and Mayer, 1977; Zerobin et al., 1977; Webel, 1978; O'Reilly et al., 1979). Preliminary data showed that when these compounds were fed at doses higher than 5 mg/animal/day for 14 to 18 days, follicular growth and ovulation were inhibited and a precisely synchronized estrus, without concurrent development of ovarian cysts, followed withdrawal of the progestin. This study was conducted to characterize further the percentage of animals displaying a post-treatment estrus (referred to here as "estrous response"), the interval to estrus and the percentage of animals with ovarian cysts (percentage cystic) among swine treated with the orally active progestin, 17-alpha-allyl-estratriene-4-9-11, 17-beta-ol-3-one, designated as allyl trenbolone (RU-2267) by Roussel-UCLAF, Paris, France. The experiment was replicated in Georgia, Illinois and Maryland to determine whether treatment effects were consistent in different geographical areas of the United States.

Materials and Methods

Gilts and sows that had displayed estrus at least once were assigned randomly to four daily doses of RU-2267: 5, 10, 20 or 40 mg (table 1). The RU-2267 was mixed in 1.8 or 2.3 kg of a corn-soybean meal diet, depending on the level of feed selected at each location. Animals were fed each morning for 18 days in groups of two to eight according to dose and were observed to ensure uniformity of consumption. Estrus was checked with a boar between 0800 and 0900 hr daily throughout the experiment. Ovaries were examined by midventral laparotomy 4 to 10 days after the post-treatment estrus or 15 to 24 days after the end of treatment in those animals that failed to display estrus. Numbers of CL formed at the post-treatment estrus (ovulation rate), follicular cysts and luteal cysts were recorded at surgery. Ovarian follicles greater than 12 mm in diameter and fluid filled with little or no luteinization were classified as follicular cysts. Ovarian follicles 10 mm or greater and fluid filled with heavy luteinization were classified as luteal cysts. Animals were classified as "cystic" if the number of follicular and(or) luteal cysts exceeded the number of CL. The experiment was replicated in three states: Georgia, Illinois and Maryland. Data were subjected to a two-way, least-squares analysis of variance, and differences between treatment means were determined by the Least Significant Difference between least-squares means with the SAS '76 statistical analysis package (Barr et al., 1976). The model included treatment, location and the location x treatment interaction.

Results and Discussion

The effects of 18 days of oral administration of 5, 10, 20 and 40 mg of RU-2267 on estrous response, interval to estrus, percentage cystic and ovulation rate are summarized in table 1. In Georgia, the estrous response among gilts fed the 5- and 10-mg doses (62%) of RU-2267 was lower (P<.05) than that among gilts fed the 20- and 40-mg doses (100%). Interval to estrus was similar for gilts fed 5 mg (5.0 ± .4 days) and those fed 10 mg (4.4 ± .4 days) of RU-2267, and for gilts fed 20 mg (5.5 ± .3 days) and those fed 40 mg (6.4 ± .3 days). However, interval to estrus was longer (P<.05) for gilts fed 20 and 40 mg of RU-2267 than for those fed 10 mg, but not those fed 5 milligrams. Interval to estrus did not differ between gilts fed 5 mg and 20 mg RU-2267, but interval to estrus was longer (P<.05) for gilts fed 40 mg than for gilts fed 5 milligrams. The percentage cystic was higher (P<.05) among gilts fed 5 mg (88%) than among gilts fed 10 mg of RU-2267. None of the gilts fed 20 or 40 mg was cystic. Therefore, the percentage cystic was greater (P<.05) at the two lower doses than at the two higher doses of RU-2267. Ovulation rate, as indicated by the number of CL at the post-treatment estrus, was similar for all gilts.

In Illinois, all gilts fed RU-2267 displayed an estrous response, except for one gilt fed 5 mg and one fed 10 mg of RU-2267. A relationship between dose of RU-2267 and interval to estrus was not evident among animals treated in Illinois. Interval to estrus did not differ between gilts fed 5 mg and 20 mg RU-2267, but interval to estrus was longer (P<.05) for gilts fed 40 mg than for gilts fed 5 milligrams. The percentage cystic was higher (P<.05) among gilts fed 5 mg (88%) than among gilts fed 10 mg (38%) of RU-2267. None of the gilts fed 20 or 40 mg was cystic. Therefore, the percentage cystic was greater (P<.05) at the two lower doses than at the two higher doses of RU-2267. Ovulation rate, as indicated by the number of CL at the post-treatment estrus, was similar for all gilts.
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TABLE 1. EFFECT OF FOUR DOSES OF RU-2267 ON ESTRUS RESPONSE (PERCENTAGE IN ESTRUS), INTERVAL TO ESTRUS, PERCENTAGE CYSTIC AND OVULATION RATE (NUMBER OF CORPORA LUTEA) IN GILTS AND SOWS AT THREE LOCATIONS

<table>
<thead>
<tr>
<th>Location</th>
<th>Dose, mg/day</th>
<th>No. of gilts and sows</th>
<th>% in estrus</th>
<th>Interval to estrus, days</th>
<th>% cystic</th>
<th>No. of CL</th>
<th>a,b,c,d,e,f</th>
</tr>
</thead>
<tbody>
<tr>
<td>Georgia</td>
<td>5</td>
<td>8</td>
<td>62\textsuperscript{d}</td>
<td>5.0 ± 4\textsuperscript{d,e}</td>
<td>88\textsuperscript{d}</td>
<td>11.0 ± 2.6</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>8</td>
<td>62\textsuperscript{d}</td>
<td>4.4 ± 4\textsuperscript{d}</td>
<td>38\textsuperscript{e}</td>
<td>15.6 ± 1.7</td>
<td></td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>8</td>
<td>100\textsuperscript{e}</td>
<td>5.5 ± 3\textsuperscript{e,f}</td>
<td>0\textsuperscript{f}</td>
<td>14.5 ± 1.3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>40</td>
<td>7</td>
<td>100\textsuperscript{e}</td>
<td>6.4 ± 3\textsuperscript{e}</td>
<td>0\textsuperscript{f}</td>
<td>15.0 ± 1.4</td>
<td></td>
</tr>
<tr>
<td>Illinois</td>
<td>5</td>
<td>6</td>
<td>83</td>
<td>4.6 ± 4\textsuperscript{d,e}</td>
<td>17</td>
<td>14.8 ± 1.7</td>
<td></td>
</tr>
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<td></td>
<td>10</td>
<td>5</td>
<td>80</td>
<td>3.5 ± 4\textsuperscript{d}</td>
<td>0</td>
<td>15.8 ± 1.7</td>
<td></td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>6</td>
<td>100</td>
<td>5.2 ± 4\textsuperscript{e}</td>
<td>0</td>
<td>14.2 ± 1.5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>40</td>
<td>6</td>
<td>100</td>
<td>5.3 ± 4\textsuperscript{e}</td>
<td>0</td>
<td>12.0 ± 1.7</td>
<td></td>
</tr>
<tr>
<td>Maryland</td>
<td>5</td>
<td>10</td>
<td>60\textsuperscript{d}</td>
<td>4.2 ± 3\textsuperscript{d}</td>
<td>70\textsuperscript{d}</td>
<td>14.3 ± 2.6</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>10</td>
<td>100\textsuperscript{e}</td>
<td>5.1 ± 2\textsuperscript{d}</td>
<td>20\textsuperscript{e}</td>
<td>17.4 ± 1.6</td>
<td></td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>10</td>
<td>100\textsuperscript{e}</td>
<td>6.0 ± 2\textsuperscript{e}</td>
<td>0\textsuperscript{e}</td>
<td>16.2 ± 1.4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>40</td>
<td>10</td>
<td>100\textsuperscript{e}</td>
<td>6.8 ± 2\textsuperscript{e}</td>
<td>0\textsuperscript{e}</td>
<td>17.1 ± 1.4</td>
<td></td>
</tr>
</tbody>
</table>

\textsuperscript{a}Least-squares mean ± SEM.
\textsuperscript{b}Ovaries were classified as "cystic" when the number of follicular and(or) luteal cysts was greater than the number of CL.
\textsuperscript{c}Animals with cystic ovaries were not included in the calculations for mean number of CL.
\textsuperscript{d,e,f}Means within a column with different superscripts differ (P<.05).

fed 10 mg than for those fed 20 or 40 milligrams. Only one gilt fed the 5-mg dose was cystic. Ovulation rate was similar for all gilts.

In Maryland, the interval to estrus differed (P<.05) between gilts (5.4 ± .3 days) and sows (6.0 ± .2 days) fed the 20-mg dose. However, because no other differences were detected, data for gilts and sows were combined. Estrous response was lower (P<.05) among gilts and sows fed 5 mg (60%) than among animals fed 10, 20 or 40 mg (100%) of RU-2267. Interval to estrus was similar for animals fed 5 mg (4.2 ± .3 days) and 10 mg (5.1 ± .2 days) of RU-2267 and similar for animals fed 20 mg (6.0 ± .2 days) and 40 mg (6.8 ± .2 days), but interval to estrus was longer (P<.05) for animals fed the 20- or 40-mg dose than for those fed the 5- or 10-mg dose of RU-2267. Seventy percent of the animals fed 5 mg and 20% of the animals fed 10 mg of RU-2267 were cystic, whereas none of the animals fed 20 or 40 mg doses was cystic. Therefore, the percentage cystic was greater (P<.05) among animals fed 5 mg than among animals fed 10, 20 or 40 mg of RU-2267. Ovulation rate was similar for all animals.

No location x treatment interactions were detected for the parameters in table 1, indicating that treatment effects were consistent between locations. Therefore, main effects of location and dose of RU-2267 were examined. Estrous response, interval to estrus, percentage cystic and ovulation rate of animals fed RU-2267 for 18 days are presented by location in table 2. Estrous response and ovulation rate were similar at the different locations, whereas interval to estrus was shorter (P<.05) and the percentage cystic lower (P<.05) in Illinois than in Georgia or Maryland.

The effect of the administration of RU-2267 for 18 days on estrous response, interval to estrus, percentage cystic and ovulation rate over all locations is presented in table 3. Estrous response was 100% among animals fed 20 or 40 mg of RU-2267, but only 67% among animals fed 5 mg and 83% among animals fed 10 mg of RU-2267. Thus, estrous response was similar for animals fed 5 and 10 mg, and for animals fed 20 and 40 mg, but was greater (P<.05) for animals fed 20 or 40 mg of RU-2267 than for those fed 5 or 10 milligrams. Interval to estrus was longer (P<.05) for animals fed 40 mg (6.1 ± .2 days) than for those fed 5 mg (4.6 ± .2 days), 10 mg (4.3 ± .2 days) or 20 mg (5.6 ± .2 days); and interval to estrus was longer (P<.05) for animals fed 20 mg than for those fed 5 or 10 mg of RU-2267. Interval to estrus was similar for animals fed 5 and 10 milligrams.
TABLE 2. EFFECT OF 5 TO 40 MG RU-2267/DAY ON ESTROUS RESPONSE (PERCENTAGE IN ESTRUS), INTERVAL TO ESTRUS, PERCENTAGE CYSTIC AND OVULATION RATE (NUMBER OF CORPORA LUTEA) AT THREE LOCATIONS

<table>
<thead>
<tr>
<th>Location</th>
<th>No. of animals</th>
<th>% in estrus</th>
<th>Interval to estrus, days</th>
<th>% cystic</th>
<th>No. of CL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Georgia</td>
<td>31</td>
<td>81</td>
<td>5.3 ± .2³</td>
<td>32³</td>
<td>14.0 ± .9</td>
</tr>
<tr>
<td>Illinois</td>
<td>23</td>
<td>91</td>
<td>4.6 ± .5³</td>
<td>4³</td>
<td>14.2 ± .8</td>
</tr>
<tr>
<td>Maryland</td>
<td>40</td>
<td>90</td>
<td>5.6 ± .2³</td>
<td>22³</td>
<td>16.2 ± .8</td>
</tr>
</tbody>
</table>

²Least-squares mean ± SEM.
³Ovaries were classified as "cystic" when the number of follicular and(or) luteal cysts was greater than the number of CL.
⁴Animals with cystic ovaries were not included in the calculations for mean number of CL.
⁵Means within a column with different superscripts differ (P<.05).

Fifty-eight percent of the animals fed 5 mg and 22% of the animals fed 10 mg were cystic, while none of the animals fed 20 or 40 mg was cystic. Therefore, the percentage cystic was greater (P<.05) among animals fed 5 mg than among animals fed 10, 20 or 40 mg of RU-2267, and greater (P<.05) among animals fed 10 mg than among those fed 20 or 40 milligrams. Ovulation rate was similar for all animals.

Except in animals that were at day 18 or 19 of the estrous cycle when treatment began, behavioral estrus was blocked by all doses of RU-2267 fed. No relationships were observed between day of cycle on which RU-2267 was initially fed and estrous response, interval to estrus, percentage cystic or ovulation rate. However, a relationship between dose of RU-2267 and estrous response, interval to estrus and percentage cystic was apparent. Estrous response was 100% among animals treated with 20 or 40 mg of RU-2267 without developing ovarian cysts, whereas estrous response was low and percentage cystic high among animals fed 5 or 10 milligrams. As the dose of RU-2267 was increased above 10 mg, the interval to estrus increased. Similar dose relationships have been reported by Webel (1978), using RU-2267, and by Mayer and Schütze (1977), Schütze and Mayer (1977) and Zerobin et al. (1977), using a different orally active progestin.

The results of this study show that when RU-2267 was fed for 18 days, the daily doses of RU-2267 most effective in synchronizing estrus and ovulation in swine were 20 and 40 mg and the minimum effective dose of RU-2267

TABLE 3. EFFECT OF FOUR DOSES OF RU-2267 ON ESTROUS RESPONSE (PERCENTAGE IN ESTRUS), INTERVAL TO ESTRUS, PERCENTAGE CYSTIC AND OVULATION RATE (NUMBER OF CORPORA LUTEA) IN GILTS AND SOWS OVER ALL LOCATIONS

<table>
<thead>
<tr>
<th>Dose, mg/day</th>
<th>No. of gilts and sows</th>
<th>% in estrus</th>
<th>Interval to estrus, days</th>
<th>% cystic</th>
<th>No. of CL</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>24</td>
<td>67³</td>
<td>4.5 ± .2³</td>
<td>58³</td>
<td>13.4 ± 1.3</td>
</tr>
<tr>
<td>10</td>
<td>23</td>
<td>83³</td>
<td>4.3 ± .2³</td>
<td>22³</td>
<td>16.2 ± .9</td>
</tr>
<tr>
<td>20</td>
<td>24</td>
<td>100²</td>
<td>5.6 ± .2³</td>
<td>0²</td>
<td>15.0 ± .8</td>
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<tr>
<td>40</td>
<td>23</td>
<td>100²</td>
<td>6.1 ± .2³</td>
<td>0²</td>
<td>14.7 ± .8</td>
</tr>
</tbody>
</table>

²Least-squares mean ± SEM.
³Ovaries were classified as "cystic" when the number of follicular and(or) luteal cysts was greater than the number of CL.
⁴Animals with cystic ovaries were not included in the calculations for mean number of CL.
⁵,⁶,⁷Means within a column with different superscripts differ (P<.05).
was between 10 and 20 milligrams. These results also show that unlike most other orally active progestins, RU-2267, given at the appropriate dose, synchronized estrus with a high degree of precision without causing development of ovarian cysts.

**Literature Cited**


