CLINICAL RESPONSE OF DAIRY COWS WITH
OVARIAN CYSTS TO GnRH\(^1,2,3,4\)

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SUMMARY

One-hundred-fourteen cows (30 Guernsey and 84 Holstein), diagnosed as having ovarian cysts via rectal palpation, were treated at random with a single IM injection of either 50, 100 or 250 \(\mu\)g synthetic gonadotropin-releasing-hormone (GnRH) or a sham injection of the carrier vehicle for GnRH (0 \(\mu\)g). All animals were from one Guernsey and three Holstein herds maintained on a reproductive herd health program where routine examinations were performed at weekly or biweekly intervals. Clinical diagnosis of ovarian cysts was based upon the finding of a single or multiple formation of smooth, fluctuant, rounded structures of 2.5 cm in diameter or larger on one or both ovaries. Response to treatment was recorded as positive if the animal established a normal estrous cycle or conceived and negative if no change in character, size or location of the cystic structure could be determined in a 2- to 4-week period. Positive response to treatment was not significantly different among the groups that received GnRH (50, 100 and 250 \(\mu\)g), but each was different from the animals receiving 0 \(\mu\)g GnRH \((P<.01)\). Positive response of cows in the 50, 100 and 250 \(\mu\)g groups was 18 of 28 (64\%), 23 of 28 (82\%) and 23 of 30 (77\%), respectively, in contrast to 6 of 28 (21\%) given 0 \(\mu\)g. For cows positively responding to treatment, the mean time in days from treatment to estrus, conception rates and services per conception for cows receiving 0, 50, 100 and 250 \(\mu\)g GnRH were 24.0, 4 of 6 (67\%) and 1.5; 22.8, 13 of 18 (72\%) and 1.6; 22.4, 20 of 23 (87\%) and 1.6; and 22.2, 17 of 23 (74\%) and 1.9, respectively. (Key Words: GnRH, Ovarian Cysts, Clinical Response.)

INTRODUCTION

Early history regarding treatment of ovarian cysts revealed utilization of manual removal or rupture of cysts at 6- to 10-day intervals until an estrous cycle developed. Recovery rates were approximately 45\% (Miller and Graves, 1932; Schjerven, 1965). Since the mid-1940’s, therapy for this syndrome has been the use of an exogenous product high in luteinizing hormone (LH) activity (Casida et al., 1944). Currently, the more popular sources of LH used are human chorionic gonadotropin (HCG) and pituitary extracts with high LH content. Exogenous LH therapy results in recovery rates of 65 to 80\% (Roberts, 1957; McKay and Thomson, 1959; Bierschwal, 1966).

The use of synthetic gonadotropin-releasing-hormone (GnRH) as a therapeutic agent for treatment of bovine ovarian follicular cysts was suggested by Kittok et al. (1973). This study was a report using multiple intravenous injections of GnRH on five affected dairy cows. The repeated intravenous dosage of GnRH was able to initiate estrous cycles in all five cows.

The objective of this experiment was to determine, under field conditions, if a single intramuscular (IM) injection of GnRH at three dose levels would be an effective treatment for ovarian cysts and, if effective, the optimum dose level. Some cows in this study were intensively studied. Results of clinical examinations and hormonal parameters of these cows are presented in a companion paper (Cantley et al., 1975).

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\(^4\) This research was conducted as part of regional research project NC-113, Endocrine Imbalances During Abnormal Reproduction in Cows.

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MATERIALS AND METHODS

One-hundred-fourteen dairy animals (30 Guernsey and 84 Holstein), diagnosed via rectal palpation as having ovarian cysts, were treated at random with an IM injection of either 50, 100 or 250 \( \mu \)g GnRH or a sham injection (0 \( \mu \)g) of the carrier vehicle (sterile water with an alcohol preservative). At the time of treatment and during subsequent rectal examinations, the investigators purposely did not know the dose of GnRH given. All animals were from one Guernsey and three Holstein herds maintained on a reproductive herd health program, the protocol of which dictated routine reproductive examinations at weekly or biweekly intervals. The basis for clinical diagnosis of ovarian cysts was the finding of a single or multiple formation of smooth, fluctuant, rounded structures on one or both ovaries of 2.5 cm in diameter or larger.

Veterinary pathologists generally recognize three types of ovarian cysts, with the most accepted classification being the following (Roberts, 1971):

- **Follicular cysts**—an anovulatory cyst, single or multiple on one or both ovaries. Clinical signs may be nymphomania or anestrus;
- **Luteal cysts**—an anovulatory cyst, usually a single structure on one ovary, with partial luteinization of the cyst. Clinical signs of anestrus are predominant;
- **Cystic corpus luteum**—ovulatory, a single structure with characteristics of a normal corpus luteum, slightly larger with fluctuation, containing a vacuole of varying size. Functionally the estrous cycle is not affected.

Since the cystic corpus luteum is ovulatory and does not usually affect progressive ovarian function, cows with cystic corpora lutea were not included in this study. Also, no attempt was made to differentiate between follicular and luteal cysts, since in many instances it is clinically impossible to differentiate the two types. In addition, treatment and response for follicular and luteal cysts have been similar.

Estrual behavior of cows with ovarian cysts prior to treatment was also used as a basis for classification as follows:

- **Anestrus**—cows more than 23 days since last observed estrus or more than 45 days postpartum with no observed estrus;
- **Nymphomania**—cows having signs of estrus with frequency of less than 17 days;
- **Unknown**—cows that had one estrus or more, but upon date of examination and diagnosis, an observed estrus was recorded less than 17 days previous to examination with no indication of nymphomania.

Findings were carefully recorded at the time of diagnosis as to location, size, number and characteristics of the cyst(s) for comparison during subsequent examination(s) for evaluation of treatment. All cows were examined via rectal palpation within 14 days following treatment and a tentative diagnosis of response to therapy was made. If at this time there was no change in location, size or character of the cyst(s), the results were termed negative and further observation was discontinued. If, however, there was a change or suspected change the cow was re-examined within 2 weeks and a final determination made at that or a later examination. Doubtful cases were re-examined 6 weeks post-treatment. Final response to treatment was recorded as positive if the animal established a normal estrous cycle or conceived. This response was chosen since some cows conceived at the first estrus following treatment. A negative response was recorded if no change in character, size or location of the cystic structure could be determined in a 2- to 4-week period.

If the response was determined to be positive, subsequent estrual behavior, ovarian changes determined per rectum and response to breeding as measured by either conceiving or failure to conceive were recorded. Conception following breeding was confirmed by rectal palpation. Additional information recorded and tabulated included the age of the animal and the number of days following parturition at the time of diagnosis and treatment. Significant differences in reproductive parameters among groups were determined by chi-square analysis.

RESULTS

Numbers and breeds of cows within the treatment groups and the age of the cows in the treatment groups were all similar (table 1). A summary of the mean days postpartum when treated is also included. Treatment was initiated on the day of diagnosis in most cases. In a few
<table>
<thead>
<tr>
<th>Item</th>
<th>GnRH treatment group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 µg</td>
</tr>
<tr>
<td>No. of animals</td>
<td>28</td>
</tr>
<tr>
<td>Breed</td>
<td></td>
</tr>
<tr>
<td>Holstein</td>
<td>16</td>
</tr>
<tr>
<td>Guernsey</td>
<td>12</td>
</tr>
<tr>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>2 to 5 year</td>
<td>21</td>
</tr>
<tr>
<td>6 to 9 year</td>
<td>5</td>
</tr>
<tr>
<td>10 year and older</td>
<td>2</td>
</tr>
<tr>
<td>Mean days from parturition to diagnosis</td>
<td>63 ± 12b</td>
</tr>
</tbody>
</table>

bTreatment was initiated on the day of diagnosis in most cases. In a few instances a subsequent examination following a tentative diagnosis was needed for confirmation. In these cases treatment was initiated upon confirmation.

A summary of pretreatment estrous behavior, size of cyst(s) and occurrence of single or multiple cysts within treatment groups is shown in table 2. Estrous behavior of the cows prior to treatment was similar among the treatment groups with 78% of the cows being anestrus. Similar distribution of cyst(s) dimensions within the treatment groups was evident. Twenty-eight percent of the cysts were 2.5 to 3.0 cm in diameter, 60% were 3.1 to 4.0 cm, and 12% were 4.1 cm or larger. Single cysts were predominant (70%) with the highest number occurring on the right ovary. Multiple cysts were detected with lower frequency and occasionally cases were found to involve both ovaries.

Subsequent fertility of cows with ovarian cysts that responded to treatment with GnRH is summarized in table 3. Response of cows receiving 50, 100 or 250 µg GnRH was not different; however, all were different from the 0 µg group (P<.01). Eighteen of 28 (64%), 23...
TABLE 3. RESPONSE OF COWS WITH OVARIAN CYSTS TO DIFFERENT LEVELS OF GnRH

<table>
<thead>
<tr>
<th>Response</th>
<th>0 µg</th>
<th>50 µg</th>
<th>100 µg</th>
<th>250 µg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>6a (21%)</td>
<td>18 (64%)</td>
<td>23 (82%)</td>
<td>23 (77%)</td>
</tr>
<tr>
<td>Negative</td>
<td>22 (79%)</td>
<td>10 (36%)</td>
<td>5 (18%)</td>
<td>7 (23%)</td>
</tr>
</tbody>
</table>

aNumber of cows.

of 28 (82%) and 23 of 30 (77%) of cows receiving 50, 100 or 250 µg GnRH, respectively, resumed progressive ovarian activity in contrast to only 6 of 28 (21%) of the cows given 0 µg GnRH. Difference in response to treatment between cows with anestrous behavior and nymphomania was not different, but the number of nymphomaniac cows in this study was small.

Subsequent fertility in cows with ovarian cysts that responded to treatment with GnRH is summarized in table 4. Mean days to first estrus following treatment was similar for all groups. Similarly, the percentage of cows conceiving, first service conceptions, services per conception and days from treatment to conception were not significantly different among groups. Four of six (67%), 13 of 18 (72%), 20 of 23 (87%) and 17 of 23 (74%) cows given 0, 50, 100 and 250 µg GnRH, respectively, conceived after treatment.

Discussion

Clinical findings of cows diagnosed as having ovarian cysts in this experiment were similar to previous studies with regard to age at time of diagnosis, size of cyst(s), occurrence of single or multiple cyst(s) and location (Bierschwal, 1966; Dawson, 1957; Roberts, 1955). The proportion of anestrous cows was slightly higher than recently reported (Bierschwal, 1966; Morrow et al., 1966).

Response to treatment with a single IM injection of either 50, 100 or 250 µg GnRH was equal to or better than results previously reported for therapeutic agents with high LH activity (Roberts, 1957; McKay and Thomson, 1959; Bierschwal, 1966). Sixty-four of 86 cows (74.4%) responded to treatment and resumed clinically normal progressive ovarian activity. Kittok et al. (1973) have reported that all five (100%) cows with ovarian follicular cysts that were treated with GnRH returned to estrus in 18 to 23 days. The higher success of treatment in that study may have been due to small numbers or the level and method of administration of GnRH. Kittok et al. (1973) gave intravenous injections of 100 µg GnRH at each of three 2-hr intervals in contrast to a single IM injection of either 50, 100 or 250 µg GnRH in

TABLE 4. SUBSEQUENT FERTILITY OF COWS WITH OVARIAN CYSTS RESPONDING TO GnRH TREATMENT

<table>
<thead>
<tr>
<th>Item</th>
<th>0 µg</th>
<th>50 µg</th>
<th>100 µg</th>
<th>250 µg</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of cows</td>
<td>28</td>
<td>28</td>
<td>28</td>
<td>30</td>
</tr>
<tr>
<td>No. cows responding to treatment</td>
<td>6</td>
<td>18</td>
<td>23</td>
<td>23</td>
</tr>
<tr>
<td>Interval from treatment to first estrus (days)</td>
<td>24 ± 4</td>
<td>23 ± 4a</td>
<td>22 ± 3</td>
<td>22 ± 3b</td>
</tr>
<tr>
<td>Total no. conceived</td>
<td>4</td>
<td>13</td>
<td>20</td>
<td>17</td>
</tr>
<tr>
<td>Days treatment to conception</td>
<td>45 ± 12</td>
<td>50 ± 7</td>
<td>43 ± 9</td>
<td>59 ± 9</td>
</tr>
<tr>
<td>No. conceiving first service</td>
<td>2</td>
<td>7</td>
<td>10</td>
<td>7</td>
</tr>
<tr>
<td>No. breedings per conception</td>
<td>1.5 ± .3</td>
<td>1.6 ± .3</td>
<td>1.6 ± .3</td>
<td>1.9 ± .3</td>
</tr>
</tbody>
</table>

aAverage days to first heat is actually 26.8 days, but two cows in this group were observed in heat at 75 and 43 days and palpation results indicated an unobserved or subclinical estrus. With removal of these two animals from the data, the average was 22.8 days.

bAverage days to first heat is actually 25.7, but two cows were observed in heat at 42 and 62 days and palpation results indicated an unobserved or subclinical estrus. With removal of these two animals from the data, the average was 22.2 days.
this study. Plasma LH was higher and was elevated longer following three intravenous injections of GnRH at 2-hr intervals as compared to a single IM injection of 50, 100 or 250 µg GnRH (Cantley et al., 1975). Differences between the groups of animals receiving 50, 100 or 250 µg GnRH were not significant although there is some indication that the 100 µg dosage may be a preferred choice in both establishment of the estrous cycle (82% positive response) and in subsequent fertility (87% conceiving of those which responded positively).

Because of its small molecular size, GnRH is not likely to stimulate an immune response reaction as may be produced by exogenous forms of LH in present use (Nakahara et al., 1961; Nakahara et al., 1962). Hence, repeated GnRH therapy should not lose its effectiveness. In addition, there should be a greatly reduced possibility of an anaphylactic reaction as with the use of exogenous forms of LH-like treatments.

Self recovery from ovarian cysts occurs with varied frequency. The earlier the occurrence of the cyst(s) in the postpartum period, the higher the frequency of self correction. Morrow et al. (1969) reported that approximately 50% of the cows developing cystic degeneration of the ovary within 45 days of calving recovered spontaneously before 60 days postpartum. Other reports vary from 13% (Johnson et al., 1966) to 29% self recovery with 30 days after diagnosis (Whitmore et al., 1974). In this study the majority of diagnoses was made more than 60 days postpartum (table 2). Six of 28 (21%) of the cows given 0 µg GnRH in this experiment returned to normal cyclic ovarian activity.

Rectal exploration of ovaries at 2 weeks post-treatment assisted in predicting response to treatment in the majority of cows. In most instances of positive response, there was a definite change in character of the cyst as evidenced by increasing firmness, loss of fluctuation and some reduction in size. In some instances a well formed corpus luteum-like structure could be found and occasionally the structure was found on the opposite ovary following treatment. It is interesting to speculate that GnRH induced an LH release that ovulated a small follicle on the ovary opposite the cyst.

Occurrence of estrus following treatment was varied and appeared to establish somewhat definite trends. Estrus occurred in the majority of cows 18 to 23 days post-treatment. However, the remaining cows tended to return to estrus in 8 to 12 or 30 to 35 days post-treatment. In cows followed intensively (Cantley et al., 1975), two instances were observed where follicular development and ovulation could be palpated at 7 to 13 days following treatment. Cysts in these two cases gradually reduced in size over a 6- to 8-day period after which follicular growth occurred. Another observation was that the cyst(s) would appear to luteinize; regress in 18 to 23 days with estrus delayed for 4 to 7 days. Accompanying this delay in estrus was the finding of clinically small inactive ovaries. Following this delayed period, follicular development, estrus, ovulation and corpus luteum formation was observed.

LITERATURE CITED

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