Bovine Somatotropin Dose Titration in Lactating Dairy Ewes.  
1. Milk Yield and Milk Composition

N. FERNANDEZ, M. RODRIGUEZ, C. PERIS, M. BARCELO,  
M. P. MOLINA, and A. TORRES  
Universidad Politécnica de Valencia  
Camino de Vera, 14-46071 Valencia, Spain

F. ADRIAENS  
Monsanto Europe  
Avenue de Tervuren 270-2725-1150  
Brussels, Belgium

ABSTRACT

Seventy-four lactating dairy ewes were injected with recombinant bST (sometribove) in a sustained-release formulation. Ewes received 0, 80, 160, or 240 mg of bST every 14 d from wk 3 to 8 of lactation (part 1) and 0, 80, or 160 mg of bST every 14 d from wk 11 to 23 of lactation (part 2). Sometribove increased milk yield over that of the controls for all treatment groups. The increase was largest for the group that was administered 160 mg of bST: milk yield was 34.1 and 53.2% and 6% FCM was 36.9 and 51.8% for parts 1 and 2 of the study, respectively. Sometribove increased milk fat during part 1 of the study, but decreased milk fat during part 2. Protein contents of milk were decreased throughout the study. For all groups, bST increased the yield of milk constituents over that of the controls. When milking frequency was reduced from twice to once daily, the difference in milk yield between control ewes and those treated with bST was maintained. Neither mastitis incidence nor milk SCC were affected by bST treatment. Recombinant bST is efficacious in increasing both actual milk yield and 6% FCM over the dose range of 80 to 240 mg/14 d without adverse effects for lactating ewes.  
(Key words: somatotropin, yield, composition, ewes)

INTRODUCTION

Many studies have been carried out with dairy cows to investigate the effects of bST administration on milk yield, milk composition, animal health, and DMI. For cows, the optimal daily dose of bST is between 25 and 35 mg/d (5, 11, 13). Although daily injections may produce better results (4, 12), the administration of sustained-release formulations of the hormone are more practical. Milk composition is not changed by bST administration (2, 5, 10, 13, 24, 33), but milk fat content can be increased at the beginning of lactation (6), and milk protein can be reduced at higher bST doses (14). Dry matter intake did not change in one study (13) of bST administration but in others (22, 31) did increase by 6 to 7% (31) over that of the controls 4 to 5 wk after the beginning of injections (22). Incidence of mastitis did not increase from bST treatment (13, 19), but milk SCC has occasionally increased (17, 27).

For lactating ewes, only a few experiments have been carried out with bST, but none has used a sustained-release formulation. For example, Spencer and Williamson (32) and Westbrook et al. (35) utilized the immunization against somatotropin release-inhibiting factor; Jordan and Shaffhausen (18), Sandles et al. (29), and McDowell et al. (21) used daily hST injections; and McDowell et al. (20) used intraarterial infusions of growth hormone. The purpose of our experiment was to evaluate a sustained-release formulation of bST at different dosages during wk 3 to 23 of lactation for Manchega ewes on milk yield, milk composition, and udder health and to investigate the impact of a reduction in milking frequency on milk yield.
MATERIALS AND METHODS

Ewes and General Procedures

Sixteen primiparous and 58 multiparous Manchega ewes were used in a dose-titration experiment at the Polytechnic University of Valencia, Spain. First lactation ewes were 23 mo old at lambing. Mating was synchronized, and all lambings (autumn) took place over a period of 15 d. At lambing, ewes were blocked by lactation number and randomly assigned to four experimental treatments. Lambs were artificially reared from birth, and ewes were milked in a parlor twice daily from lambing to wk 18 postpartum and once daily thereafter until the end of the lactation at wk 23. Ewes were fed in three groups according to milk yield, and rations were balanced to meet minimum recommendations for 2.0, 1.5, and 1.0 U/d (8), consisting of straw, alfalfa hay, orange pulp, beet root pulp, brewers grains, and a commercial concentrate for lactating ewes.

Treatment

Treatments consisted of a subcutaneous injection of recombinant bST (sometribove; Monsanto Europe, Brussels, Belgium) in a prolonged-release formulation designed to deliver bST constantly over a 14-d period in cows. Treatment was administered subcutaneously in the postscapular region on Saturday mornings, alternating sides each time. The controls remained un.injected. Record 0 was taken on the Thursday preceding the first injection (a Saturday).

Part 1: First Dose Titration

From wk 3 until and including wk 10 postpartum (first part of the lactation), ewes received three injections of 0, 80, 160, or 240 mg of bST at 14-d intervals. After the third injection (wk 6 postpartum), there was a 4-wk period without injections to observe the yield decline posttreatment.

Part 2: Second Dose Titration

Injections continued from wk 11 until wk 23 postpartum (second part of the lactation) without further interruptions. Because no incremental benefit over the group receiving injections of 160 mg of bST/14 d was seen for the group receiving 240 mg of bST/14 d, the ewes of the group receiving 240 mg of bST/14 d were assigned to the remaining groups (0, 80, and 160 mg of bST/14 d) at random.

Experimental Data and Sample Collection

Milk yield was recorded twice a week (on Tuesdays and Thursdays) throughout the lactation, and milk samples were taken from consecutive milkings from 24-h period to analyze milk fat, protein, lactose, and DM content with an infrared analyzer (D400; Brann+Luebbe, Nordejtedt, Germany) and SCC by a Fossomatic 90 (Foss Electric, Hillerød, Denmark).

Ewes were weighed and scored for body condition at lambing, at the beginning of bST injections, and at 28-d intervals thereafter. A five-point scoring system (0 = very thin to 5 = very fat) was used to assess body condition (28).

Milk yield at 6% FCM was calculated from unadjusted milk yield (UMY) and milk fat percentage (F) according to the following equation (23):

\[ 6\% \text{ FCM} = \text{UMY} \cdot (0.106F + 0.362). \]

Statistical Analysis

The statistical design for analyzing the effects on daily milk yield, 6% FCM, and milk components (fat, protein, lactose, and DM) was a model of covariance with the following model:

\[ Y = \mu + D_i + L_j + DL_{ij} + \beta(X_{ijk} - \bar{X}) + e_{ijk} \]

where

- \( Y \) = observations for dependent variables,
- \( \mu \) = overall mean,
- \( D_i \) = effect of bST dose \( i \) (\( n = 4 \) or 3),
- \( L_j \) = lactation (primiparous vs. multiparous) effect,
- \( \beta(X_{ijk} - \bar{X}) \) = covariant adjustment from pretreatment period,
SOMATOTROPIN FOR LACTATING EWES

\[ DL_{ij} = \text{dose} \times \text{lactation number interaction, and} \]
\[ \varepsilon_{ijk} = \text{residual error.} \]

Covariance was used to adjust experimental data, and records –3, –2, –1, and 0 (wk -2 to 0; before initial bST treatment) were used as covariant for records +1 to +12 (part 1). Record +16 was used as covariant for the rest of the treatment (part 2). Lactation number factor and interaction between dose and lactation number factors were considered in a preliminary analysis and were pooled with the error term because they were insignificant \((P > .20)\).

The experimental design for studying the effects on body score, live BW, and log SCC was a mixed model of ANOVA as follows:

\[ Y = \mu + D_i + R_k + DR_{ik} + I_j(D_i) + \varepsilon_{ijk} \]

where new elements are

\[ R_k = \text{record,} \]
\[ DR_{ik} = \text{dose} \times \text{record interaction, and} \]
\[ I_j(D_i) = \text{individual effect within dose.} \]

All models were analyzed with the GLM procedure of SAS (30). Differences among treatment means were evaluated using linear and quadratic contrasts for milk yield, 6% FCM, milk components, and SCC. Separation of means for a significant \((P < .05)\) main effect was accomplished with the PDIF option of the least squares procedures (a pairwise t test) for body score and live BW.

TABLE 1. Least squares means for milk yield and composition from ewes administered sustained-release bST during wk 3 to 8 of lactation.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>0 mg</th>
<th>80 mg</th>
<th>160 mg</th>
<th>240 mg</th>
<th>SE</th>
<th>Phase 1</th>
<th>Phase 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>20</td>
<td>18</td>
<td>18</td>
<td>18</td>
<td></td>
<td>1042</td>
<td>-240</td>
</tr>
<tr>
<td>Milk, ml/d</td>
<td>997</td>
<td>1198</td>
<td>1337</td>
<td>1298</td>
<td>12.08</td>
<td>.000</td>
<td>.000</td>
</tr>
<tr>
<td>6% FCM, ml/d</td>
<td>1072</td>
<td>1301</td>
<td>1467</td>
<td>1452</td>
<td>14.91</td>
<td>.000</td>
<td>.000</td>
</tr>
<tr>
<td>Milk fat, %</td>
<td>6.7</td>
<td>6.8</td>
<td>6.9</td>
<td>7.1</td>
<td>.049</td>
<td>1.3</td>
<td>.088</td>
</tr>
<tr>
<td>Milk protein, %</td>
<td>5.2</td>
<td>5.1</td>
<td>4.9</td>
<td>4.9</td>
<td>.022</td>
<td>-1.10</td>
<td>.10</td>
</tr>
<tr>
<td>Milk lactose, %</td>
<td>5.1</td>
<td>5.1</td>
<td>5.1</td>
<td>5.1</td>
<td>.016</td>
<td>.00</td>
<td>.061</td>
</tr>
<tr>
<td>Milk DM, %</td>
<td>17.6</td>
<td>17.0</td>
<td>17.3</td>
<td>17.5</td>
<td>.062</td>
<td>.00</td>
<td>.061</td>
</tr>
<tr>
<td>SCC(^1)</td>
<td>5.26</td>
<td>5.17</td>
<td>5.24</td>
<td>5.24</td>
<td>.013</td>
<td>.01</td>
<td>.003</td>
</tr>
</tbody>
</table>

\(^1\)Log\(_{10}\)-transformed.

\(^2\)Contrasts: phase 1 = linear, and phase 2 = quadratic.

RESULTS AND DISCUSSION

Milk Yield and Milk Composition

Linear components for milk yield and 6% FCM were positive and significant, and quadratic components were negative and significant for both parts of the experiment (Tables 1 and 2). Nevertheless, the linear and quadratic components of milk composition, and their significance, were variable, depending on which part of the experiment is being considered.

Administration of 80, 160, and 240 mg of bST/14 d increased milk and 6% FCM yield from wk +1 to +6 (wk 3 to 8 of lactation) over that of the controls (Table 1). An incremental milk yield response occurred for the group that was administered 160 mg of bST/14 d over that for the groups administered 80 and 240 mg of bST/14 d. As a result, the experimental group receiving 240 mg of bST/14 d was removed from part 2 of the study.

Administration of 80 and 160 mg of bST/14 d during part 2 again increased milk and 6% FCM over that of the controls (Table 2). Milk yield and FCM were not affected by parity.

During part 1 of the study, milk fat was increased by administration of bST/14 d and tended to increase with the dose rate. During part 2, milk fat increased progressively for all groups as lactation progressed; however, for ewes treated with bST, milk fat decreased slightly. The increase in milk fat after the first bST injections was also observed by Eppard et al. (14), Bitman et al. (6), and McDowell et al.
TABLE 1. Least squares means for milk composition from ewes administered sustained-release bST during wk 11 to 23 of lactation.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>0 mg /14 d</th>
<th>80 mg /14 d</th>
<th>160 mg /14 d</th>
<th>SE</th>
<th>Phase 1</th>
<th>Phase 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>20</td>
<td>20</td>
<td>22</td>
<td></td>
<td>10.66</td>
<td>-181.00</td>
</tr>
<tr>
<td>Milk, ml/d</td>
<td>618</td>
<td>873</td>
<td>947</td>
<td></td>
<td>329.00</td>
<td>-203.00</td>
</tr>
<tr>
<td>6% FCM, ml/d</td>
<td>770</td>
<td>1071</td>
<td>1169</td>
<td></td>
<td>399.00</td>
<td>-203.00</td>
</tr>
<tr>
<td>Milk fat, %</td>
<td>8.6</td>
<td>8.4</td>
<td>8.4</td>
<td>.052</td>
<td>-20.41</td>
<td>.20 .324</td>
</tr>
<tr>
<td>Milk protein, %</td>
<td>6.0</td>
<td>5.5</td>
<td>5.2</td>
<td>.022</td>
<td>-80.00</td>
<td>.20 .000</td>
</tr>
<tr>
<td>Milk lactose, %</td>
<td>4.7</td>
<td>4.9</td>
<td>4.9</td>
<td>.015</td>
<td>.20 .000</td>
<td>-20.000</td>
</tr>
<tr>
<td>Milk DM, %</td>
<td>19.7</td>
<td>19.1</td>
<td>18.8</td>
<td>.053</td>
<td>-1.00</td>
<td>.20 .100</td>
</tr>
<tr>
<td>SCC1</td>
<td>5.24</td>
<td>5.20</td>
<td>5.18</td>
<td>.008</td>
<td>-.06</td>
<td>.02 .060</td>
</tr>
</tbody>
</table>

1Log_{10}-transformed.
2Contrasts: phase 1 = linear, and phase 2 = quadratic.

(21), who attributed this increase to an increase in long-chain fatty acids from body reserves mobilized when cows were in negative energy balance.

Milk protein also increased for all groups as lactation progressed but was more pronounced for the control group. Milk protein content was decreased by the administration of bST/14 d during both parts 1 and 2 of the study and clearly tended to decrease further with incremental bST doses. The reduction in milk protein content with increasing bST dosage was also observed for cows by Eppard et al. (14) and for ewes by Sandles et al. (29). Sandles et al. (29) explained that this increase was due to the large milk yield increase (18%), compared with that for the control group, an increase that was far less than that obtained in the present experiment.

Treatment with bST did not affect milk lactose during the first part of the study (5.1%; Table 1) but increased milk lactose in the second part (Table 2).

Milk DM followed a pattern similar to that for milk protein. For all groups, DM substantially increased as lactation progressed but was lowered in a dose-related fashion by bST treatment.

However, milk yield components had a positive and significant linear component and a negative and significant quadratic component in parts 1 (Table 3) and 2 (Table 4) of the experiment.

Administration of sustained-release bST at all the doses studied resulted in an increase in fat, protein, lactose, and DM yields during both part 1 and part 2 of this study (Tables 3 and 4). The group that was administered 160 mg bST had the highest DM yield during both parts of the study.

TABLE 2. Least squares means for milk yield from ewes administered sustained-release bST during wk 11 to 23 of lactation.

<table>
<thead>
<tr>
<th>Ewes and milk component</th>
<th>0 mg /14 d</th>
<th>80 mg /14 d</th>
<th>160 mg /14 d</th>
<th>SE</th>
<th>Phase 1</th>
<th>Phase 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ewes no.</td>
<td>20</td>
<td>18</td>
<td>18</td>
<td></td>
<td>1.04</td>
<td>-15.00</td>
</tr>
<tr>
<td>Milk fat, g/d</td>
<td>66</td>
<td>80</td>
<td>92</td>
<td>91</td>
<td>87 .000</td>
<td>-15 .00</td>
</tr>
<tr>
<td>Milk protein, g/d</td>
<td>51</td>
<td>59</td>
<td>65</td>
<td>64</td>
<td>45 .000</td>
<td>-9 .000</td>
</tr>
<tr>
<td>Milk lactose, g/d</td>
<td>51</td>
<td>61</td>
<td>69</td>
<td>66</td>
<td>.72</td>
<td>53 .000</td>
</tr>
<tr>
<td>Milk DM, g/d</td>
<td>173</td>
<td>207</td>
<td>229</td>
<td>225</td>
<td>178 .000</td>
<td>-38 .000</td>
</tr>
</tbody>
</table>

1Contrasts: phase 1 = linear, and phase 2 = quadratic.

SOMATOTROPIN FOR LACTATING EWES

TABLE 4. Least squares means for milk yield components from ewes administered sustained-release bST during wk 11 to 23 of lactation.

<table>
<thead>
<tr>
<th>Ewes and milk component</th>
<th>bST</th>
<th>Contrasts</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 mg 80 mg 160 mg</td>
<td>SE Phase 1 P Phase 2 P</td>
</tr>
<tr>
<td>Ewes, no.</td>
<td>/14 d /14 d /14 d</td>
<td></td>
</tr>
<tr>
<td>Milk fat, g/d</td>
<td>20 20 22 20 20 22</td>
<td>.90 27 .000 -15 .000</td>
</tr>
<tr>
<td>Milk protein, g/d</td>
<td>36 47 48 36 47 48</td>
<td>.52 12 .000 -10 .000</td>
</tr>
<tr>
<td>Milk lactose, g/d</td>
<td>30 44 48 30 44 48</td>
<td>.59 18 .000 -10 .000</td>
</tr>
<tr>
<td>Milk DM, g/d</td>
<td>119 165 176 119 165 176</td>
<td>1.91 57 .000 -35 .000</td>
</tr>
</tbody>
</table>

1Contrasts: phase 1 = linear, and phase 2 = quadratic.

mg of bST/14 d showed the largest increase over the controls, but was similar in fat and DM yields to the group administered 240 mg of bST/14 d.

Two ewes from the group administered 0 mg of bST/14 d, 3 from the group administered 80 mg of bST/14 d, 2 from the group administered 160 mg of bST/14 d, and 0 from the group administered 240 mg of bST/14 d required treatment for mastitis. Milk SCC were similar for the groups receiving 0, 160, and 240 mg of bST/14 d but higher than for the group receiving 80 mg of bST/14 d in part 1 (Table 1). During part 2 of the study, SCC were higher for the controls than for the groups receiving 80 and 160 mg of bST/14 d (Table 2).

Based on the present study, the optimal dose of the sustained-release bST preparation used was 160 mg of bST/14 d. This dose is equivalent to 11.4 mg/d and is much lower than the optimal dose (25 to 27 mg/d) reported by Downer et al. (13) and Bauman et al. (5) for cows, but much higher by metabolic weight (7.3 mg of bST/kg.75) than for cows (2.7 mg of bST/kg.75). The difference in milk yield response observed between the groups receiving 80 and 160 mg of bST/14 d would suggest the testing of further intermediate bST doses to define the optimal dosage further.

Injections of 160 mg of bST/14 d increased 6% FCM 36.9 and 51.8%, fat yield 39.4 and 54.0%, protein yield 28.0 and 33.3%, lactose yield 35.3 and 60.0%, and DM yield 32.4 and 47.9% over the controls in parts 1 and 2 of the study, respectively. The influence of stage of lactation was also observed by Phipps et al. (25), Arambel et al. (1), and Thomas et al. (34), who saw a higher response to bST administration during the second part of the lactation.

Milk Yield and Constituent Graphs

Milk yield, fat, and protein percentage are presented in Figure 1; lactose percentage, DM percentage, and SCC are presented in Figure 2. Milk yield immediately increased after the first bST injection for all doses. Milk yield dropped to the level of the controls during wk 9 and 10 (records 12 to 16) as one injection was skipped. When injections were resumed after record +16, milk yield again increased to 1.1 L/d, .3 L/d over that of the controls for groups receiving 80 and 160 mg of bST/14 d. This second peak was lower than the one during part 1 of this study but was sustained until milking was reduced to once daily milking, resulting in a very abrupt drop in yield. The low capacity of the udder cistern in the Manchega breed is probably responsible for this decline. In a study by Fernández et al. (15), milk yield of Manchega ewes decreased 52% when milking frequency changed from twice to once daily, but Casu et al. (9), utilizing the Sarda breed, which has greater udder cistern capacity, found that yield decreased only 26% under the same conditions.

Graphs of the milk yield of the groups injected with bST in the present study show undulation similar to the pattern previously described by Barbano et al. (3).

The graph of milk fat (Figure 1) shows a similar tendency for all the groups during periods of twice daily milking, after the initial milk fat increase described for the groups receiving 160 and 240 mg of bST/14 d. When
Figure 1. Unadjusted mean yields for milk, fat, and protein in response to biweekly administration of sustained-release bST (arrow) for ewes beginning wk 3 postpartum.
Figure 2. Unadjusted mean lactose, DM, and SCC in response to biweekly administration of sustained-release bST (arrow) for ewes beginning wk 3 postpartum.

ewes were switched from twice to once daily milking, milk fat content increased substantially as a result of the decline in milk yield.

Figure 1 shows that protein percentage for the control was higher than for groups receiving bST but was similar 14 d after the third bST injection during part 1 (records +12 to +16). Milk protein was affected in an undulating manner, opposite in direction to that of milk yield.

Milk lactose was similar for all groups during the first 8 wk of the lactation but lower in the control group thereafter; milk lactose declined substantially after the change to once daily milking (Figure 2).

Milk DM content followed a pattern similar to that for protein, being inversely related to milk yield and higher for the control group after record +16 (wk 10 of lactation).

Milk SCC decreased during the first weeks of lactation and increased again toward the end

Figure 3. Least square means for body score and live BW in response to biweekly administration of sustained-release bST (arrow) for ewes beginning wk 3 postpartum. Means with different letters (a, b, c) differ (P < .05).

of lactation as milk yield declined. The same SCC evolution throughout the lactation was observed by Gonzalo et al. (16) for ewes and by Reneau (26) for cows.

Live BW and Body Condition

All groups started the experiment (wk 0; Figure 3) with a body condition score close to 3, which is considered normal by Reneau (26) for cows. Two ewes in the highest yielding group (160 mg of bST/14 d) gained body condition more slowly than did the other groups, and the ewes in the lowest yielding group (control) started to gain condition by wk 4 of lactation, when milk yield was about 1 L/d. The group receiving 240 mg of bST/14 d lost most body condition after the first injections, explaining the pronounced increase in milk fat observed in that group at that time (Figure 1).

Body weight, however, increased more rapidly for the groups treated with bST than for the controls. The differences in BW, body condition, and milk yield among groups suggest a higher DMI and ruminal contents for the bST groups. This result is consistent with the results of Sandles et al. (29), who reported an increment in DMI in ewes 2 wk after the beginning of bST injections.

CONCLUSIONS

This experiment compared different doses of a sustained-release bST and the impact of decreasing the number of milkings on milk yield. In conclusion, all doses studied increased milk and FCM yield in ewes. The bST-treated ewes gained body condition more slowly but were heavier than the controls. Administration of bST initially increased milk fat, decreased milk protein, maintained milk lactose, but increased the yield of all milk constituents.

No adverse effects were observed on udder health at any of the doses.

A change from twice to once daily milking resulted in a similar drop in milk yield in all groups, but the difference was maintained between control ewes and ewes treated with bST. The optimal dose of sustained-release bST in this experiment was 160 mg of bST/14 d.

ACKNOWLEDGMENTS

This work forms part of the project GAN-90-0570, financed by the Comisión Interministerial de Ciencia y Tecnología.

REFERENCES


