Effect of Somidobove Sustained Release Administration on the Lactation Performance of Dairy Cows

R. K. MCGUFFEY, R. P. BASSON, and D. L. SNYDER
Lilly Research Laboratories
Eli Lilly and Company
Greenfield, IN 46140

E. BLOCK
MacDonald College
McGill University
Ste. Anne de Bellevue, PQ
Canada H9X 1C0

J. H. HARRISON
Washington State University
Puyallup 98371

A. H. RAKES
North Carolina State University
Raleigh 27695-7621

R. S. EMERY
Michigan State University
East Lansing 48824

L. D. MULLER
The Pennsylvania State University
University Park 16802

ABSTRACT

Lactation performance was determined on 190 multiparous Holsteins from five herds supplemented with 0, 320, 640, or 960 mg of somidobove every 28 d. The experiment consisted of 21 d of pretreatment and treatment periods of various lengths, depending upon stage of lactation of animals at first administration. Somidobove beginning in early (28 to 45 d in milk), mid (111 to 166 d in milk), or late (166 to 334 d in milk) stages of lactation consisted of 9, 6, or 3 administrations. Milk and 3.5% FCM yields were increased by each dose of somidobove in all stages. Milk composition and dry matter and energy intakes were similar among treatments within stage. Milk to DMI ratio and milk energy to net energy intake ratio were improved by somidobove. Gain was positive for all treatments, but less in somidobove-supplemented cows. Lower body weight and condition score at the completion of somidobove treatment resulted. For early cows, days to first estrus and days to first breeding were similar; however, total number of inseminations for cows receiving somidobove was twofold greater than control, resulting in a longer calving interval. Results demonstrated efficacy of somidobove administered every 28 d to lactating dairy cattle for increased milk yield.
(**Key words**: somidobove, lactation, somatotropin)

Abbreviation key: NADA = new animal drug application, NEI = net energy intake, PP = postpartum.

INTRODUCTION

Extensive research has been conducted administering recombinantly derived bovine so-

Received May 14, 1990
Accepted November 1, 1990.

matotropin to the lactating dairy cow. Results of this research have led to a greater understanding of how various factors influence milk production (6, 14, 17). These findings will be influential for the successful adoption of this technology by dairy farmers.

For dairy farmers to derive benefits from this technology, a manufacturer of bST must receive approval for a new animal drug application (NADA) from the US Food and Drug Administration. One of several sections in a NADA is efficacy and safety of the compound in the target species. Efficacy requirements include a dose-titration experiment conducted in a minimum of three geographical locations using at least three nonzero doses along with an untreated control group (8). Conditions of the experiment are designed to approach potential field use as closely as possible.

Development of the protocol described here occurred following initial studies described by McGuffey et al. (13). The current studies were conducted to determine the effect of incremental doses of somidobove on lactation performance of multiparous dairy cows when somidobove supplementation began in either early, mid, or late stages of lactation.

MATERIALS AND METHODS

A total of 190 multiparous Holsteins at five locations were assigned to treatment (Table 1). Days postpartum (PP) at the beginning of pretreatment were used to classify cows by three stages of lactation as follows: early, 7 to 24 d PP; mid, 90 to 145 d PP; and late, 145 to 313 d PP.

The experiment consisted of 21 d of pretreatment and treatment for 252, 168, or 84 d for cows in early, mid, and late lactation, respectively. Within each stage of lactation, average daily milk production during pretreatment and calendar date of assignment were used to form blocks of four cows. Within blocks, treatments were assigned randomly. Experimental treatment was a subcutaneous administration of somidobove (13) at one of four doses: 0, 320, 640, or 960 mg given at 28-d intervals in a formulation volume of 6.9, 2.3, 4.6, and 6.9 ml, respectively. Treatments were administered subcutaneously on alternate sides of the animal using a 14-gauge needle. At four trial locations, somidobove was administered in the scapular region; the fifth location administered somidobove in the neck.

TABLE 1. Number of cows used at each location.

		No. of cows receiving somidobove, mg/28 d			
Location	Stage[1]	0	320	640	960
Michigan	Early	3	3	3	3
	Mid	4	3	3	3
	Late	3	5	3	3
North Carolina	Early	3	3	3	3
	Mid	3	3	4	3
	Late	4	3	3	4
Pennsylvania	Early	3	4	4	3
	Mid	3	4	4	3
	Late	3	3	3	3
Quebec	Early	3	4	3	4
	Mid	2	2	2	2
	Late	4	3	4	3
Washington	Early	3	3	3	3
	Mid	3	3	3	3
	Late	3	3	3	3
Total	Early	15	17	16	16
	Mid	15	15	16	14
	Late	17	17	16	16
	All	47	49	48	46

[1]Stage of lactation at initiation of somidobove: early, 28 to 45 d postpartum (PP); mid, 111 to 166 d PP; late, 166 to 334 d PP.

TABLE 2. Feedstuffs used for ration formulation at each trial site.

Location	Forage	Concentrates
Michigan	Alfalfa hay and haylage, corn silage	High moisture ear corn, customized supplement
North Carolina	Corn silage	Concentrate mixture, whole cottonseeds
Pennsylvania	Corn silage, alfalfa hay and haylage	High moisture shelled corn, customized supplement
Quebec	Alfalfa haylage, corn silage	Corn grain, high moisture ear corn, soybean meal
Washington	Corn silage, corn-sunflower silage, alfalfa hay, grass silage	Customized supplement, whole cottonseeds

At each location, up to three rations were formulated from locally available feedstuffs (Table 2). Three rations, designated low, medium, and high energy, were designed to correspond in nutrient content to Rations II, III, and IV, respectively, described in Table 3 of NRC (16). All rations were fed for ad libitum intake as total mixed rations. Initially, cows in early lactation were fed the high ration during pretreatment and for the first 84 d of treatment. Initial ration assignments for cows in mid and late lactation were based on their average daily milk production at the beginning of pretreatment. All cows within a block were offered the same ration during pretreatment and for the first 84 d of treatment. Ration assignments during the second and third 84 d of treatment were according to average daily milk during the last 28 d of the previous 84-d period. Rations were changed from high to medium when cows averaged less than 29.0 kg/d during the 28-d period. Likewise, rations were changed from medium to low when cows averaged less than 20.9 kg/d during the 28-d period. At no time was a change made from high to low, from low to medium, or from medium to high. Rations were sampled weekly and composited for chemical analysis at 4-wk intervals. Composites were analyzed for DM, CP, fat, NDF, ADF, Ca, and P (1). Results for each ration at each location are presented in Table 3.

Cows were milked twice daily at all locations, and yield was recorded. Milk was sampled twice weekly during pretreatment and weekly during treatment from both milkings and composited proportional to milk yield. Fat, protein, total solids, and somatic cells were determined on all composite samples. Feed intake was recorded daily. Body weight and body condition score (scale of 0 to 5) (15) were determined at the beginning and end of pretreatment, on the 1st d of treatment administration, and at 28 d intervals thereafter. Body weight at the end of treatment was measured on 2 consecutive d.

Yield (3.5% FCM) was calculated as milk yield × .4324 + fat yield × 16.218. Efficiency of production was calculated as a) Milk / DMI (wt/wt) b) NE_{milk} / NEI, and c) ([NE_{main} + NE_{milk} + NE_{wchg}] / NEI), where DMI is dry matter intake (kg/d), NE_{main} is ($BW^{.75}$ × .08 Mcal/kg, NE_{milk} is SCM (22) × .75 Mcal/kg, NE_{wchg} is weight gain × 5.12 Mcal/kg (4.92 if weight gain was negative), and NEI is net energy intake (Mcal/d). For statistical purposes, SCC was converted to $\log_{10}$, analyzed, and converted back to a whole number.

At each location, standard herd measures were followed for mastitis control and treatment, herd health, detection of estrus, and breeding. All breedings were by artificial insemination. Days to first estrus, days to first breeding, number of inseminations, and calving interval were estimated to measure reproductive effects of treatments. Weight and sex of all calves were recorded at birth.

Bartlett's test of chi-square values (10) was used to test for heterogenous variance for eight measured parameters among the five trial locations. Among the three stages, only five of the 24 chi-square analyses exceeded the critical value of 14.9 for 4 df (location). These included milk fat percentage, DMI, and body condition score for early lactation cows, milk yield for midlactation cows, and DMI for late lactation cows. This analysis showed no strong indication of heterogeneity of variance among measured parameters. As a result, an unweighted analysis was conducted on both measured and calculated variables. Statistical analysis was performed independently on parameters from the stages of lactation and in a combined model in which stage with two degrees of freedom represented a source of variation. The sources of variation in the statistical model and degrees of freedom for each source are shown in Table 4. Covariate analysis was used on all measured parameters except body condition score. All analyses were performed using the general linear models procedure of SAS (19).

RESULTS

Ten cows removed from the experiment are listed in Table 5 with reasons for removal. Number removed was 4, 4, 1, and 1 for 0, 320, 640, and 960 mg somidobove, respectively. Overall, 94.7% of the cows completed at least two-thirds of the treatment period, the required minimum time for inclusion in the data summary.

Milk production and milk composition are presented for each stage of lactation in Table 6. Milk yield was increased by somidobove regardless of when somidobove administration

TABLE 3. Chemical composition of rations.[1]

	Location				
Ration	MI	NC	PA	PQ	WA
	(%)				
High					
DM, %	56.9	47.7	49.9	51.0	63.1
EE	3.5	5.3	5.9	3.0	5.4
CP	17.0	18.8	16.8	18.6	19.3
NDF	50.9	39.3	29.9	35.5	42.7
ADF	16.4	21.5	19.4	21.8	25.0
Ash	6.4	7.6	7.3	ND[3]	8.5
Ca	.90	.80	.93	.71	1.01
P	.56	.49	.55	.39	.62
NE_L,[2] Mcal/kg	1.69	1.87	1.66	1.67	1.66
Medium					
DM, %	52.6	39.3	46.4	47.1	57.2
EE	3.3	4.8	5.4	3.2	4.0
CP	16.8	16.6	16.1	17.0	18.6
NDF	50.6	43.4	32.7	39.0	45.9
ADF	19.1	23.5	22.0	24.9	29.0
Ash	6.5	7.3	7.8	ND	9.3
Ca	.87	.67	1.09	.68	1.15
P	.52	.43	.50	.39	.50
NE_L,[2] Mcal/kg	1.63	1.79	1.61	1.64	1.58
Low					
DM, %	Not fed	40.3	Not fed	45.0	Not fed
EE		4.3		2.9	
CP		17.4		15.3	
NDF		41.4		43.2	
ADF		19.6		31.7	
Ash		6.1		ND	
Ca		.41		.95	
P		.44		.43	
NE_L,[2] Mcal/kg		1.76		1.55	

[1]All components of DM expressed as a percentage.

[2]NE_L calculated from NRC (16).

[3]Not determined.

TABLE 4. Analysis of variance: sources and degrees of freedom by stage of lactation and for stages combined.

Source	Stage of lactation			
	Early	Mid	Late	All
	(df)			
Location (L)	4	4	4	4
Stage (S)	. . .	. . .	. . .	2
L × S	. . .	. . .	. . .	8
Replicate (L)	12	11	13	. . .
Replicate (L × S)	. . .	. . .	. . .	36
Treatment (T)	3	3	3	3
T × L	12	12	12	. . .
T × S	. . .	. . .	. . .	6
T (L × S)	. . .	. . .	. . .	36
Covariate	1	1	1	1
Residual	29	24	28	83
Total	61	55	61	179

began. Milk yield increase above control among stages ranged from 1.9 to 3.8, from 4.7 to 5.6, and from 4.3 to 6.1 kg/d for cows receiving 320, 640, and 960 mg, respectively. For each dose of somidobove, the greatest increase occurred with cows beginning somidobove administration in early lactation. The improvement from control cows was significant ($P < .01$) for all dosages of somidobove when all stages were combined into one analysis.

Differences in milk composition as the result of somidobove administration were minor and showed no consistent meaningful biological trends. A means comparison of control versus each somidobove dose identified 2 out of 48 comparisons for fat, protein, and total solids percentage and SCC as being different ($P < .05$). For this number of comparisons, one should expect 2 to 3 comparisons to show statistical significance by chance alone. Overall, somidobove had no effect on milk composition or SCC regardless of stage of lactation when administration was initiated.

Average daily milk yields during the 28-d injection interval are shown in Figure 1 for each dose of somidobove at each stage of lactation. The milk production response to somidobove began on the day immediately following administration and peaked 4 to 8 d after injection. Peak milk was maintained until d 9 to 10 of the interval before decreasing. By d 17 to 20 after administration, milk yield of somidobove cows had returned to d 1 values. In early lactation cows, but not midlactation or late lactation cows, milk yield at d 28 was higher for somidobove cows than for control cows, suggesting a somidobove effect on persistency of milk production.

Average 3.5% FCM by stage of lactation for each dose of somidobove is in Table 6. There was a significant increase in 3.5% FCM by all doses of somidobove. There was an increasing response in 3.5% FCM to increasing amounts of somidobove, with the exception of cows in late lactation receiving 960 mg. Increase in 3.5% FCM by 320, 640, and 960 mg of somidobove across all stages ranged from 2.3 to 3.7, 4.4 to 4.6, and 4.2 to 6.0 kg/d, respectively. Average 3.5% FCM yields for control cows and for cows receiving 640 mg of somidobove are shown for each stage of lactation in Figure 2. The repeatability of the re-

TABLE 5. Removals of cows from herd and reasons.

Location	Cow no.	S[1]	Somidobove	Reason for removal
			(mg/28 d)	
Michigan	1864	Mid	0	Assigned wrong ration initially
	1960	Late	320	Abortion
	1970	Late	320	Mastitis during pretreatment
North Carolina	3777	Late	960	Abortion
Pennsylvania	90	Early	320	Teat injury
	133	Early	0	Hardware
	50	Mid	320	Periuterine abscess
	88	Mid	640	Injured teat
Quebec	438	Late	0	Mastitis
Washington	540	Mid	0	Intestinal blockage

[1]Stage of lactation when somidobove administration began.

sponse to somidobove is illustrated both within each stage and among all stages of lactation.

Three single degree of freedom contrasts, 0 vs. 320 to 960, 0 vs. 640 to 960, and 0 vs. 960, were used to describe the dose response curve for milk and 3.5% FCM in the combined analysis. These contrasts describe dose-response curves with a plateau at 320 mg, a plateau at 640 mg, or a linear response to somidobove, respectively. Treatment sums of squares for milk and 3.5% FCM were 611.1 and 589.5. The contrast, 0 vs. 640 to 960 accounted for 97.3 to 97.5% of treatment sums of squares, whereas 81 to 93% of treatment sums of squares were accounted for in other contrasts. This analysis indicates a diminishing returns response for both milk and 3.5% FCM at or beyond the 640 mg dose of somidobove.

There were no differences among doses of somidobove in either DMI or NEI within any stage of lactation or overall (Table 7). On a limited basis, cows were changed to lower energy rations because continued high milk production necessitated that cows remain on high energy rations. All ration changes occurred at

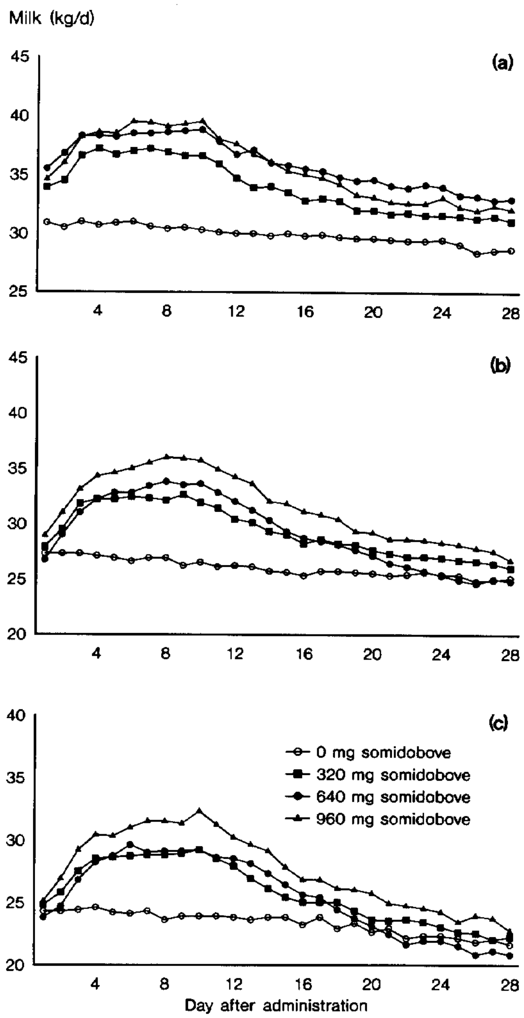

Figure 1. Average milk production (kg/d) of cows receiving somidobove calculated for each day of the 28-d administration period using all periods: a) early, b) mid, and c) late.

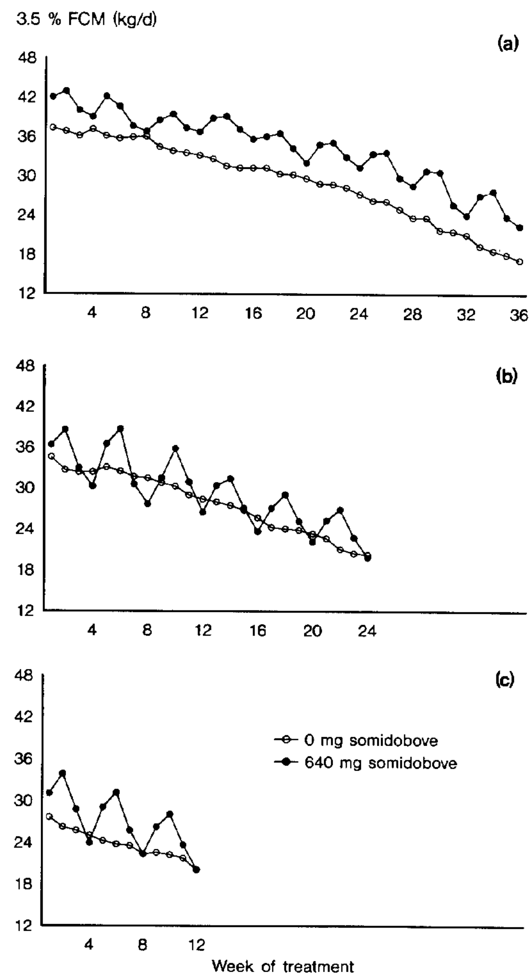

Figure 2. Average 3.5% FCM (kg/d) by week of cows receiving 0 or 640 mg of somidobove administered beginning in a) early, b) mid, or c) late lactation.

the beginning of the last 84 d of the experiment.

Ending body weights of cows receiving somidobove were less than untreated in all cases (Table 7). When all stages were combined, cows receiving somidobove weighed less ($P < .05$) than untreated controls. Differences in ending body weight are reflected in daily gain estimates for each treatment. Daily gain was reduced 20 to 50% by somidobove among stages compared with controls. Overall, daily gain was reduced ($P < .05$) by .17 to .22 kg/d in cows receiving somidobove compared with untreated controls.

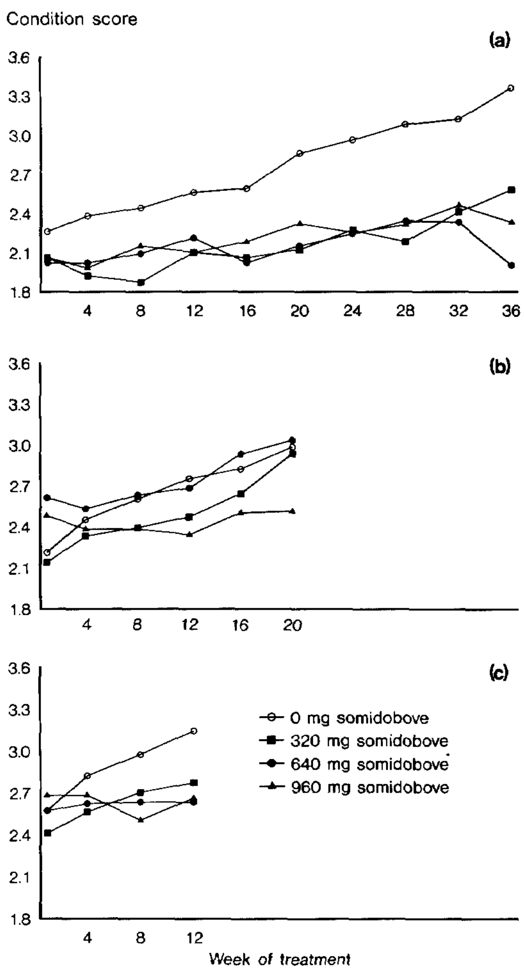

Figure 3. Changes in body condition score during administration of somidobove beginning in a) early, b) mid, or c) late lactation.

Ending body condition score for cows receiving somidobove was less than untreated controls in early ($P < .07$), mid ($P < .25$), and late ($P < .05$) stages of lactation (Table 7). The most consistent reduction occurred in cows receiving somidobove early. Cows in this stage began somidobove with lower condition scores than in other stages (Figure 3).

Measures of efficiency of production are shown in Table 8. Milk to DMI ratio, a measure of gross feed efficiency, was greater ($P < .01$) for all cows receiving somidobove. Improvement by stage ranged from 13.5% for cows receiving 960 mg in early lactation to 28.2% for cows receiving 640 mg somidobove in late lactation. Milk energy to NEI ratio, a measure of energy partitioning into milk, was numerically greater for cows receiving somidobove when each stage was considered independently. Combining stages resulted in a 13.7% increase ($P < .01$) in partitioning of NEI into milk energy. There were no differences in biological efficiency of net energy utilization ($[NE_{main} + NE_{milk} + NE_{wchg}]$ / NEI) in cows receiving somidobove within stage of lactation or when stages were combined.

Health observations are shown in Table 9. Most observations for cows occurred in the early lactation group, and fewest occurred in the late lactation group. Reproduction was the primary health observation, with mastitis second, in terms of number of cows affected when somidobove began in early lactation.

In midlactation cows, reproduction was also the primary need for veterinary attention. All cows in this stage were required to have been bred at least once prior to the experiment. As a result of random assignment, 3 of 15, 6 of 15, 7 of 16, and 10 of 14 cows assigned to 0, 320, 640, and 960 mg of somidobove, respectively, were not pregnant prior to the experiment. For this reason, a greater number of cows receiving somidobove might be expected to have reproductive-related observations (as was the case). Mastitis was the second most prevalent category requiring attention for midlactation cows. There were few nonmastitis health related observations in late cows.

Breeding information is presented in Table 10 for early cows receiving somidobove. Days to first recorded estrus and days to first breeding were similar among doses of somidobove. Total number of inseminations was more than twice as great in the somidobove groups compared with untreated control. Eleven cows were bred five or more times; one cow received 13 inseminations. Two of the five trial locations (Québec and Pennsylvania) accounted for 60% of the inseminations in the somidobove group. Calving interval of somidobove dose groups was extended 27 to 68 d compared with untreated control.

Information on subsequent calving of early lactation cows is shown in Table 11. Total number of cows that calved was similar. There was no difference among somidobove doses in weight of calves at birth. Of the six sets of twins, two sets occurred in the 320-mg group and four sets occurred in the 960-mg group.

DISCUSSION

Results of the large-scale field study confirmed previous observations on the galactopoietic properties of somidobove in a sustained release formulation (13). In McGuffey et al. (13), the increase in 3.5% FCM yield was significantly greater at 960 mg than with 320 or 640 mg of somidobove; however, treatment in earlier studies was for only 84 d. In the present studies, milk yield of cows receiving 640 and

TABLE 6. Milk production, milk composition, and SCC of cows receiving somidobove beginning in different stages of lactation.[1]

		Somidobove, mg/28 d				
Item	Stage[2]	0	320	640	960	SE
Milk, kg/d	Early	29.7	33.5[a]	35.3[b]	35.8[b]	1.3
	Mid	25.7	29.3[a]	30.3[b]	31.2[b]	1.7
	Late	23.0	24.9	27.7[b]	27.3[b]	1.1
	All	26.5	29.3[b]	30.8[b]	31.5[b]	.8
Fat, %	Early	3.46	3.45	3.33	3.48	.13
	Mid	3.77	3.68	3.70	3.72	.11
	Late	3.83	3.92	3.86	3.82	.12
	All	3.39	3.68	3.65	3.37	.07
Protein, %	Early	3.23	3.23	3.22	3.29	.05
	Mid	3.41	3.36	3.34	3.34	.05
	Late	3.51	3.52	3.46	3.47	.06
	All	3.39	3.37	3.34	3.36	.03
Total solids, %	Early	12.16	12.16	12.01	12.22	.17
	Mid	12.59	12.46	12.53	12.51	.15
	Late	12.60	12.71	12.76	12.64	.14
	All	12.46	12.44	12.45	12.44	.09
SCC × 100	Early	79.4	91.2	109.6	95.5	
	Mid	128.8	97.7	97.7[a]	112.2	
	Late	104.7	93.3	100.0	107.2	
	All	100.0	93.3	102.3	107.2	
3.5% FCM, kg/d	Early	29.5	33.0[a]	34.0[b]	35.3[b]	1.4
	Mid	26.3	29.9[a]	30.9[b]	31.9[b]	1.9
	Late	24.2	26.6	28.7[b]	28.5[b]	1.2
	All	26.9	29.9[b]	31.1[b]	31.9[b]	.8

[a]Means is different from 0 treatment ($P < .05$).

[b]Means is different from 0 treatment ($P < .01$).

[1]Least squares means.

[2]Stage of lactation when somidobove administration began.

960 mg of somidobove was not different within three stages of lactation when treatment was initiated.

Somewhat surprising were the similar increases in 3.5% FCM obtained from somidobove regardless of stage of lactation at initiation of treatment. A comparison of the daily yield profile during the 28-d period suggests that initiation of somidobove prior to establishing peak milk yield may have increased persistency for the remainder of lactation, whereas initiation of somidobove in mid and late stages did not affect persistency. Some of the advantage in bST initiation prior to peak may be related to the association increasing peak milk yield has on milk production over the remainder of lactation (4).

The daily milk yield profile during the 28-d interval was similar among stages of lactation in which somidobove was initiated. Peak milk was obtained 3 to 5 d after administration and was maintained for 7 to 10 d before declining to preadministration yields by 17 to 20 d after administration. The shape of the response curve undoubtedly reflects release of somidobove from the formulation. Results from our laboratory (unpublished observations) suggest that plasma somatotropin concentration in cows supplemented with somidobove returns to preadministration values by 17 to 21 d. Schams (20) reported similar characteristics of somidobove from the sustained release formulation. Milk yield during the last 7 d of the 28-d interval appeared to follow the expected milk yield based upon lactation curve analysis of control and treated cows in mid and late stages.

The pattern of milk response over the 28-d interval suggests more frequent injections might result in a greater galactopoietic response

TABLE 7. Dry matter intake, net energy intake, ending body weight, weight gain, and ending condition score of cows receiving somidobove beginning in different stages of lactation.[1]

Item	Stage[2]	Somidobove, mg/28 d				SE
		0	320	640	960	
Dry matter intake, kg/d	Early	22.3	21.6	23.0	23.4	.9
	Mid	20.9	21.3	21.9	21.7	.8
	Late	21.3	20.1	20.6	21.7	1.0
	All	21.4	21.1	21.8	22.2	.5
Net energy intake, Mcal/d	Early	37.7	36.7	39.2	39.7	1.4
	Mid	35.3	36.2	37.1	36.9	1.3
	Late	35.8	33.9	34.7	36.6	1.6
	All	36.1	35.8	37.0	37.6	.8
Ending body weight, kg/d	Early	689	663	658	662	16
	Mid	712	693	698	678[b]	12
	Late	715	708	693	700	10
	All	705	688[a]	683[a]	681[a]	7
Weight gain, kg/d	Early	.37	.24	.25	.24	
	Mid	.51	.38	.41	.26[a]	
	Late	.85	.56[a]	.55[a]	.55[a]	
	All	.57	.39[b]	.40[b]	.35[b]	
Ending condition score	Early	3.11	2.51[a]	2.41[a]	2.46[a]	
	Mid	3.13	2.74	3.09	2.58	
	Late	3.31	2.94	2.73[a]	2.64[b]	
	All	3.18	2.73[a]	2.74[b]	2.56[b]	

[a]Mean is different from 0 treatment ($P < .05$).

[b]Mean is different from 0 treatment ($P < .01$).

[1]Least squares means.

[2]Stage of lactation when somidobove administration began.

TABLE 8. Measures of efficiency of milk production of cows receiving somidobove beginning in different stages of lactation.[1]

Item	Stage[2]	Somidobove, mg/28 d				SE
		0	320	640	960	
Milk:DMI	Early	1.373	1.601	1.580	1.559	.075
	Mid	1.232	1.373[a]	1.353[a]	1.427[b]	.061
	Late	1.102	1.276	1.413[b]	1.265	.093
	All	1.239	1.416[b]	1.450[b]	1.421[b]	.045
Milk energy:NEI	Early	.559	.651	.629	.631	.032
	Mid	.530	.575	.570	.600[b]	.023
	Late	.478	.556	.616[b]	.552	.042
	All	.523	.594[b]	.605[b]	.595[b]	.020
Efficiency of energy utilization[3]	Early	.942	.976	.923	.951	.048
	Mid	.932	.946	.925	.926	.026
	Late	.943	.951	1.045	.961	.075
	All	.937	.960	.964	.944	.031

[a]Mean is different from 0 treatment ($P < .05$).

[b]Mean is different from 0 treatment ($P < .01$).

[1]Least squares means.

[2]Stage of lactation when somidobove administration began.

[3]$[NE_{main} + NE_{milk} + NE_{wchg}]$ / NEI where NE_{main} is $BW^{.75} \times .08$ Mcal/kg; NE_{milk} is SCM × .75 Mcal/kg; NE_{wchg} is weight gain × 5.12 Mcal/kg; NEI is net energy intake (Mcal/d).

TABLE 9. Number of cows observed for various conditions while receiving somidobove beginning in different stages of lactation.

Category	Stage[1]	No. of cows receiving somidobove, mg/28 d			
		0	320	640	960
None	Early	6	3	1	3
	Mid	7	4	6	5
	Late	14	10	10	11
Digestive	Early	2	2	1	3
	Mid	5	3	3	2
	Late	0	0	1	1
Feet and legs	Early	1	1	1	2
	Mid	0	2	2	1
	Late	0	0	4	0
Mammary	Early	1	3	4	2
	Mid	2	2	1	2
	Late	1	1	1	1
Mastitis	Early	6	9	4	7
	Mid	2	2	5	4
	Late	2	4	3	2
Reproductive	Early	7	10	13	9
	Mid	2	6	3	4
	Late	0	1	. . .	1

[1]Stage of lactation when somidobove administration began.

to somidobove. However, milk yield increase in the current trials was similar to that reported previously from our laboratory (13) and from comparable complete lactation experiments that injected bST more frequently (5, 11). Chalupa and Galligan (6) concluded that the average 3.5% FCM increase noted in most bST experiments ranged from 4 to 5 kg/d.

The hyperbolic shape of the dose-titration curve from the current study agrees with reports of other dose studies with bST administered as daily injections (2, 5, 21). Expressed as a daily dosage, 320, 640, and 960 mg correspond to 11.4, 22.8, and 34.2 mg/d. These doses are comparable with those used in other studies with more frequent injections (2, 5, 11, 13, 21). The diminishing returns at the upper doses suggest that some factors other than dose of bST limit milk production response.

Considerable emphasis has been placed on increased feed intake as a means for providing the extra nutrients to meet requirements for the extra milk produced as a result of bST administration. In most reports, differences in energy intake between untreated and bST-treated groups account for 50 to 75% of the extra energy secreted in milk (2, 3, 5, 13, 21). Much of the difference in feed (energy) intake re-

TABLE 10. Reproductive performance of cows administered somidobove beginning at 28 to 45 d postpartum and continuing for 252 d.

	Somidobove, mg/28 d			
Item	0	320	640	960
No. of cows	15	17	16	16
Days to first estrus				
MI	68.7	69.3	115.7	72.3
NC	103.3	63.3	112.7	79.7
PA	60.3	52.0	66.0	36.7
PQ	45.0	48.0	49.7	61.0
WA	35.7	49.7	61.0	53.3
Mean	62.6	56.2	80.1	60.6
Days to first breeding				
MI	69.7	69.3	63.0	73.0
NC	103.3	64.0	141.7	80.0
PA	68.0	63.5	80.5	79.3
PQ	88.7	83.8	67.7	67.5
WA	70.0	63.7	78.3	70.0
Mean	79.9	68.5	85.9	74.4
Number of inseminations				
MI	4	5	4	7
NC	6	5	10	9
PA	3	17	13	15
PQ	6	22	15	15
WA	5	13	7	5
Total	24	62	49	51
Calving interval				
MI	379.0	328.0	406.0	392.0
MC	362.0	383.3	. . .[1]	363.5
PA	330.2	424.0	460.5	. . .[1]
PQ	403.3	497.0	471.3	469.8
WA	366.0	442.0	432.0	369.0
Mean	375.5	420.8	443.8	402.3

[1]No cows calved in these groups.

ported in the literature is the result of three factors: 1) increased feed intake, 2) maintenance of higher feed intake over a longer part of lactation by bST-supplemented cows, and 3) decreased feed intake by untreated cows as lactation progresses. Differences in feed intake between groups may be more related to maintaining high feed intake in bST-supplemented cows and decreasing feed intake by untreated cows rather than to increased feed intake by treated cows. For example, Bauman et al. (2) reported a difference in NEI of 5.1 Mcal/d between untreated cows and cows receiving 27 mg/d bST during 188 d. Actual increase in NEI for bST-supplemented cows occurred beginning in wk 5 of supplementation but remained in the range of 38 to 40 Mcal/d for most of the 188 d. However, untreated cows maintained NEI for about 10 wk before declining steadily from approximately 38 to 25 Mcal/d at the end of the study. This decline in NEI began when net energy balance reached a maximum (about wk 10). Although energy density was a possible confounding factor with milk production in that study, the authors concluded that, because average week of rations shift was wk 20 or greater for all treatment groups, energy intake was not confounded by diet.

Bauman et al. (2) suggested that feed intake regulation was more likely associated with tissue metabolism than with bST per se. When tissues have a high metabolic rate, such as for milk production, feed intake is pulled to meet nutrient demands. When balance becomes positive, intake is able to provide for nutrient needs and declines as nutrient intake exceeds demand. Demand may include tissue repletion.

Reasons for lack of difference in DMI or NEI between control and bST-supplemented cows in this study are not immediately clear. The lack of difference in feed intake (early cows) may have been due in part to the relatively low body condition for all cows. Under these conditions, tissue metabolism may have remained high throughout much of the injection period, resulting in a higher persistency of DMI for all groups. What is apparent is the different way in which calories were partitioned among energy-requiring functions in untreated cows and cows receiving somidobove. Both ending body weight and condition score were higher for untreated cows compared with cows receiving somidobove. Differences in ending body weight are reflected in different rates of gain between untreated cows compared with cows receiving somidobove. The other part of this partitioning is illustrated by higher partitioning efficiency to milk by somidobove-treated cows.

The one health category that appeared to be related to somidobove supplementation was reproduction in early lactation of cows. The number of cows affected was increased in each dose group but was not different among doses in cows in midlactation or late lactation. The increased incidence in reproductive related observations in cows receiving somidobove did not appear to affect onset of cycling or expression of estrus adversely but did increase inseminations per pregnancy and calving interval. Initiation of somidobove approximately 80 d in milk had no effect on these parameters in other studies [Wilkinson, personal communication; (7, 9)]. Delaying initiation of somidobove until the last two-thirds of lactation may reduce any

TABLE 11. Number of cows calving, birth weight, and incidence of twins by sex of calves born to cows after receiving somidobove for 252 d of lactation.

Item	Somidobove, mg/28 d			
	0	320	640	960
No. cows calving	10	13	13	11
Single births	10	11	13	7
Male, kg	41.4 (6)[1]	48.0 (6)	45.1 (9)	49.6 (5)
Females, kg	43.8 (4)	41.5 (5)	39.4 (4)	42.0 (2)
Twins	...	2	...	4
Male, kg	...	35.0 (4)	...	29.6 (3)
Female, kg	...	...	...	29.0 (5)

[1]Number of calves is shown in parentheses.

reproduction and breeding difficulties. Feed intake capacity of the cow would be maximized as well.

Overall, fertility and calf weight were not affected. Of interest was the presence of twins in the somidobove cows only. This trend has been observed in other studies (18, 23), but a definitive cause and effect has not been established. However, German workers recently reported an increase in the number of transferable ova recovered from superovulated cows that had received somidobove 5 to 7 d prior to superovulation therapy (12).

The results of previous work with somidobove in a sustained release vehicle have now been extended to cows receiving bST for longer periods of the lactation. The results demonstrate that 640 mg administered every 28 d provides similar increases in 3.5% FCM whether administration began in early, mid, or late lactation. The decision to use somidobove or any bST should be based on objectives of the user. Use beginning about 30 d PP would provide maximum milk production during the lactation. If maintaining a 12 to 13 mo calving interval is the objective, then initiation of use at 80 to 100 d PP may be desirable. In either case, body weight and body condition should be evaluated near the end of lactation to ensure adequate time for repletion of body reserves.

ACKNOWLEDGMENTS

The authors gratefully acknowledge the technical assistance of Nancy J. Williams, W. James Johnson, J. S. Liesman, L. A. Foster, Martin Leonard, Robert Riley, Kevin Loney, D. C. Young, Carol Burns, Tom Craig, H. B. Green, R. N. Meyer, and R. D. Muller during collection and summary of data.

REFERENCES

1 Association of Official Analytical Chemists. 1980. Official methods of analysis. 13th ed. AOAC, Washington, DC.

2 Bauman, D. E., P. J. Eppard, M. J. DeGeeter, and G. M. Lanza. 1985. Responses of high producing dairy cows to long-term treatment with pituitary somatotropin and recombinant somatotropin. J. Dairy Sci. 68: 1352.

3 Bauman, D. E., D. L. Hard, B. A. Crooker, M. S. Partridge, K. Garrick, L. D. Sandles, H. N. Erb, S. E. Franson, G. F. Hartnell, and R. L. Hintz. 1989. Long-term evaluation of a prolonged-release formulation of n-methionyl bovine somatotropin in lactating dairy cows. J. Dairy Sci. 72:642.

4 Broster, W. H., V. J. Broster, T. Smith, and J. W. Siviter. 1975. Experiments on the nutrition of the dairy heifer. IX. Food utilization in lactation. J. Agric. Sci. (Camb.) 84:173.

5 Chalupa, W., L. Baird, C. Soderholm, D. L. Palmquist, R. Hemken, D. Otterby, R. Annexstad, B. Vecchiarelli, R. Harmon, A. Sinha, J. Linn, W. Hansen, F. Ehle, P. Schneider, and R. Eggert. 1987. Responses of dairy cows to somatotropin. J. Dairy Sci. 70(Suppl. 1): 176.(Abstr.)

6 Chalupa, W., and D. T. Galligan. 1989. Nutritional implications of somatotropin for lactating cows. J. Dairy Sci. 72:2510.

7 Chalupa, W., A. Kutches, D. Swager, T. Lehenbauer, B. Vecchiarelli, R. Shaver, and E. Robb. 1988. Responses of cows in a commercial dairy to somatotropin. J. Dairy Sci. 71(Suppl. 1):210.(Abstr.)

8 Code of Federal Regulations. 1987. Food and drugs. 21:514(8). Natl. Archiv. Records Admin., US Govt. Printing Office, Washington, DC.

9 Eppard, P. J., D. E. Bauman, C. R. Curtis, H. N. Erb, G. M. Lanza, and M. J. DeGeeter. 1987. Effect of 188 day treatment with somatotropin on health and reproductive performance of lactating dairy cows. J. Dairy Sci. 70:582.

10 Gill. J. L. 1978. Design and analysis of experiments in the animal and medical sciences. The Iowa State Univ. Press, Ames.

11 Hard, D. L., W. J. Cole, S. E. Franson, W. A. Samuels, D. E. Bauman, H. N. Erb, J. T Huber, and R. C. Lamb. 1988. Effect of long-term sometribove, USAN (recombinant methionyl bovine somatotropin), treatment in a prolonged release system on milk yield, animal health and reproductive performance pooled across four sites. J. Dairy Sci. 71:(Suppl. 1):210.(Abstr.)

12 Herrler, A., E. Farries, and H. Niemann. 1990. A trial to stimulate insulin-like growth factor I levels to improve superovulatory response in dairy cows. Theriogenology 33:248. (Abstr.)

13 McGuffey, R. K., H. B. Green, R. P. Basson, and T. H. Ferguson. 1990. Lactation response of dairy cows receiving bovine somatotropin via daily injections or in a sustained release vehicle. J. Dairy Sci. 73:763.

14 McGuffey, R. K, and J.I.D. Wilkinson. 1991. Nutritional implications of bovine somatotropin for the lactating dairy cow. J. Dairy Sci. 74(Suppl.2):63.

15 Mulvaney, P. 1977. Dairy cattle condition scoring. National Institute for Research in Dairying. Paper No. 4468. Shinfield, Reading, Berkshire, Engl.

16 National Research Council. 1978. Nutrient requirements of dairy cattle. 5th ed. Natl. Acad. Sci., Washington, DC.

17 Peel, C. J., and D. E. Bauman. 1987. Somatotropin and lactation. J. Dairy Sci. 70:474.

18 Phipps, R. H. 1989. A review of the influence of somatotropin on health, reproduction and welfare in lactating dairy cows. Page 88 *in* Uses of somatotropin in livestock production. K. Sjersen, M. Vestergaard, and A Nieman-Sorensen, ed. Elsevier Applied Science, London, Engl.

19 SAS® User's Guide: Statistics, Version 82.3. SAS Inst., Inc., Cary, NC.

20 Schams, D. 1989. Somatotropin and related peptides in milk. Page 192 *in* Uses of somatotropin in livestock production. K. Sjersen, M. Vestergaard, and A Nieman-Sorensen, ed. Elsevier Applied Science, London, Engl.

21 Soderholm, C. G., D. E. Otterby, J. G. Linn, F. E. Ehle, J. E. Wheaton, W. P. Hansen, and R. J. Annexstad. 1988. Effects of different doses of recombinant bovine somatotropin on milk production, body composition, and physiological parameters. J. Dairy Sci. 71:355.

22 Tyrrell, H. F., and J. T. Reid. 1965. Prediction of the energy value of cow's milk. J. Dairy Sci. 48:1215.

23 Wilkinson, J.I.D., and R. K. McGuffey. 1989. Recent developments in somatotropin research. 4th Int. Symp. Modern Cattle Prod. German Cattle Breeders Assoc., Giessen, Germany.