

Effects of Boostin-250 Supplementation on Milk Production and Health of Dairy Cows

Yo-Han Kim and Doo Kim¹

College of Veterinary Medicine & Institute of Veterinary Science, Kangwon National University, Chuncheon 200-701, Korea

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Abstract : The recombinant bovine somatotropin (rbST) has been used for increasing milk production of dairy cows without adverse health effects. This study was conducted to compare effects of supplementation with Boostin[®]-250 containing 250 mg of rbST on milk production with those of Posilac[®] and Boostin[®]-S. And safety of rbST supplementation on target animals was also observed. Each twenty-five lactating dairy cows were assigned randomly to one of four groups. Boostin[®]-250 and vehicle (control) were administered weekly. Boostin[®]-S and Posilac[®] were administered two week intervals. Milk yield, milk components, milk somatic cell count, health status, and body condition score of cows were examined. Supplementation with Posilac[®], Boostin[®]-S, and Boostin[®]-250 induced more milk yield than control group by 2.9 kg/day (12.3%), 4.2 kg/day (17.9%), and 4.1 kg/day (17.4%), respectively. There was a significant difference in milk yield among three rbST treatment groups and control group ($\alpha = 0.05$). The rbST supplementation did not increase the incidence of clinical mastitis and milk somatic cell counts. Supplementation with rbST did not significantly affect milk components (milk fat, protein, and solid not fat). The rbST supplementation of the dairy cows after peak milk yield did not cause negative effect on BCS. However, some cows less than 100 days in milking had decreased BCSs after rbST supplementation. In conclusion, milk production in 250 mg of rbST administered cows every week was similar to that of 500 mg of rbST administered cows every 2 weeks. And supplementation of 250 mg of rbST every week could reduce metabolic stress in cows.

Key words : rbST, 250 mg, dairy cows, milk yield, health.

Introduction

Somatotropin is a kind of growth hormone releasing from anterior pituitary gland (14). Recombinant bovine somatotropin (rbST) is a synthetically derived hormone that may be identical to naturally occurring bovine growth hormone, or slightly modified by the addition of extra amino acids (14). The use of rbST to increase milk production in dairy cows in the USA was approved by the US Food and Drug Administration in 1992. After the rbST product was approved for sale in the USA, many countries such as Republic of Korea, South Africa, and Brazil were also approved its' use in their countries. The 75% of Wisconsin dairy producers with over 200 cows used rbST (2). Lactation response to sustained release formulation of rbST is linear up to 750 mg every 14 days (17). And supplementation with a sustained release formulation containing 500 mg of rbST at 14-day intervals has increased milk production by an average of 3 to 5 kg/d (1,17,23).

Catastrophic health effects have been postulated to occur with rbST supplementation of dairy cows. Adverse health effects including increased risk of adverse reproductive effects, ketosis, fatty liver, clinical mastitis, feet, and leg problems,

injections site reactions, udder edema, and other general health effects were all proposed as possible side effects of rbST use (13). These postulated catastrophic effects were not based on actual data but rather on the presumption that rbST was an acute effector of lipolysis or overtly caused stress. However, various studies have demonstrated that the health risks of dairy cows were manageable (1) and the use of rbST in dairy cows has virtually no impact on human health (10).

Metabolic disorders would be most likely to occur during the first few days of rbST use (i.e., increases milk prior to change in voluntary intake) and in the farms in which inadequacies in the overall quality of the management (6). To reduce the metabolic stress of dairy cows, the precise individual feeding management and the low dose of rbST supplementation were needed.

This study was conducted to compare effect of weekly supplementation with Boostin[®]-250 containing 250 mg of rbST on milk production with those of Posilac[®] and Boostin[®]-S. And safety of rbST supplementation on target animals was also observed.

Materials and Methods

Materials

Boostin[®]-S formulation (LG Life Science Co. LTD, Seoul,

¹Corresponding author.
E-mail : kimdoo@kangwon.ac.kr

Korea; Lot No. BSS09047) contains alanyl bST 500 mg in vehicle which has composed with 1,200 mg vitamin E acetate and 300 mg of lecithin.

Boostin[®]-250 formulation (LG Life Science Co. LTD, Seoul, Korea; Lot No. BSR09030) contains alanyl bST 250 mg in vehicle which has composed with 1,200 mg vitamin E acetate and 300 mg of lecithin.

Posilac[®] (500 mg of Sometribove zinc suspension; ELANCO Animal Health, IN, USA; Lot No. 08G31/SK).

Vehicle formulation (LG Life Science Co. LTD) contains only vehicle which has composed with 1,200 mg vitamin E acetate and 300 mg of lecithin.

Animals

The one hundred lactating Holstein cows from one commercial dairy herd in Kyunggi Province were used for this experiment. The herd was selected based on the following criteria: 1) willingness to comply with the experimental protocol, 2) practice of a mastitis control program that includes premilking and postmilking teat dipping as well as dry cow treatment of all cows, and 3) availability of a computerized system for recording events of cows and daily individual milk yield. The cows were reared in free stalls. All cows received *ad libitum* TMR, containing corn silage, alfalfa and timothy hay, steam-flaked corn, whole cott seed, soy bean meal, beet pulp, marine protein, calcium salts of palm fatty acids, minerals, and vitamins. Diet was formulated to meet the nutrient requirements for lactating Holstein cows weighing 650 kg and producing 35 kg of 3.5% FCM (NRC, 2001).

Experimental design

Cows were assigned randomly to one of four groups. Cows in Group I were administered subcutaneously the formulation (LG Life Science Co. LTD) which has only vehicle in left and right side of ischiorectal fossa by turns, weekly. Cows in Group II were administered subcutaneously Posilac[®] in left and right side of ischiorectal fossa by turns, biweekly. Cows in Group III were administered subcutaneously Boostin[®]-S in left and right side of ischiorectal fossa by turns, biweekly. Cows in Group IV were administered subcutaneously Boostin[®]-250 in left and right side of ischiorectal fossa by turns, weekly.

One to three cows of each group were excluded from the experiment as cows had clinical mastitis and whose milk yield

were not recorded during experiment. Milk yield, parity, and lactation days of cows in each group at beginning of experiment were summarized in Table 1.

Measurements

Milk yield

Milk yields were recorded at each milking (twice daily) from 2 week prior to treatment to 2 weeks after the end of experimental period.

Milk components and somatic cell count

The milk samples were collected on the day of initiation of experiment and every 4 weeks during the experiment, and analyzed by Milko-Scan 4000 (Foss Electric Co, Denmark) for milk fat, protein, solid not fat, and somatic cell count (SCC).

Observation of health status of cows

Animals were observed daily for general health status and clinical mastitis.

Body condition score

Body condition of all cows was scored on the day of study enrollment at 2 week intervals throughout the experimental period. Scores were based on the five-point scale (1 = very thin to 5 = very fat).

Statistical analysis

Statistical analyses were conducted using SAS PACKAGE (STAT User's Guide, Version 9, Cary NC, USA). Milk yield was analyzed using the GLM Procedure,

$$Y_{ijklm} = \mu + P_i + D_j + T_k + \beta X_l + \epsilon_{ijklm}$$

y_{ijklm} : the observation in a treatment period,

μ : overall mean,

P_i : the effect of i th parity ($i = 1, 2, 3, 4$),

D_j : the effect of j th lactation stage ($j = 1, 2, 3, 4$),

T_k : the effect of k th treatment ($k = 1, 2, 3, 4$),

β : regression coefficient

X_l : the effect of l th milk production of 2 weeks before rbST treatment (continuous variate),

ϵ_{ijklm} : a random error term $\sim N(0, \sigma^2)$.

The mean of 2-week pretreatment value for milk yield was included in the model as a covariate to reduce experimental variation. Significance of means among groups on milk com-

Table 1. Number of cows, milk yield, parity and lactation day of each group at pretreatment

Variable	Group I	Group II	Group III	Group IV
n*	23	22	24	23
Milk yield (kg/d)	27.8 ± 8.7	24.9 ± 7.4	28.4 ± 7.0	26.3 ± 6.3
Parity (year)	1.9 ± 1.3	1.6 ± 0.9	1.8 ± 1.1	2.1 ± 1.1
Lactation day	243.1 ± 129.5	236.7 ± 128.6	211.0 ± 114.1	205.5 ± 116.6

*Cows were excluded from the experiment as cows had clinical mastitis or other diseases and whose milk yield were not recorded during experiment.

ponents, SCC, and body condition score were tested, using Duncan's multiple range test. A statistical test was considered significant if it had $\alpha = 0.05$ unless indicated otherwise.

Results

Milk production

Milk production of each rbST supplementation groups for 20 weeks of experimental period was shown in Table 2. Supplementation means for milk yield were adjusted by covariance for the 2 weeks prior to treatment. Least squares mean for milk yield of each group (from Group I to Group IV) was 23.5 ± 0.6 kg/day, 26.4 ± 0.6 kg/day, 27.7 ± 0.6 kg/day, and 27.6 ± 0.6 kg/day, respectively. Supplementation with Posilac[®], Boostin[®]-S formulation, and Boostin[®]-250 formulation induced more milk yield than control Group I by 2.9 kg/day (12.3%), 4.2 kg/day (17.9%), and 4.1 kg/day (17.4%), respectively. There was significant difference in milk yield between all rbST supplementation groups and control group ($\alpha = 0.05$) (Table 2).

Control cows (Group I) exhibited a trend of progressive decreasing of milk yield throughout the experiment (Fig 1). After the rbST supplementation, the pattern of milk production for each supplementation groups was cyclic and nearly consistent although there was a variability in milk yield in

each day. In Group II which was administered Posilac[®], the pattern of milk production started with a increase in milk production by day 6 of each administration and then the pattern ended with a decrease until the subsequent administration. In Group III which was administered Boostin[®]-S formulation, the pattern of milk production consisted of a progressive increase in milk production from day 2 of each administration to a peak on day 7, and then a progressive decrease was observed until the 14th day of administration. In Group IV, which was administered Boostin[®]-250 formulation, the pattern of milk production consisted of a progressive increase in milk production from day 1 of each administration to a peak on day 3-4, and then a progressive decrease was observed until the 7th day of administration. Milk production of 1 week after Boostin[®]-250 administration was higher than that of previous administration. And fluctuation of milk production in Boostin[®]-250 group was smaller than that of Boostin[®]-S group (Fig 1).

Mastitis and general health

The effect of rbST on mastitis was evaluated by the incidence of clinical mastitis and milk SCC. The experimental herd had well equipped milking parlor and practiced mastitis control program that includes pre- and post-milking teat dipping as well as dry cow treatment of all cows. During exper-

Table 2. Least squares means for milk yield of cows administered with rbST for 20 weeks

Variable	Group I	Group II	Group III	Group IV
n*	23	22	24	23
Milk yield**, kg/d (LS mean \pm SE)	$23.5 \pm 0.6^{***}$	26.4 ± 0.6^b	27.7 ± 0.6^b	27.6 ± 0.6^b
Increase in milk yield than Group I (kg/d)		2.9	4.2	4.1
Comparison with Group I (%)		112.3	117.9	117.4

*One to three cows in each group were excluded from the experiment because of clinical mastitis.

**Means were covariate-adjusted for the pretreatment period.

***Means with different superscript in the same row differ significantly ($\alpha = 0.05$).

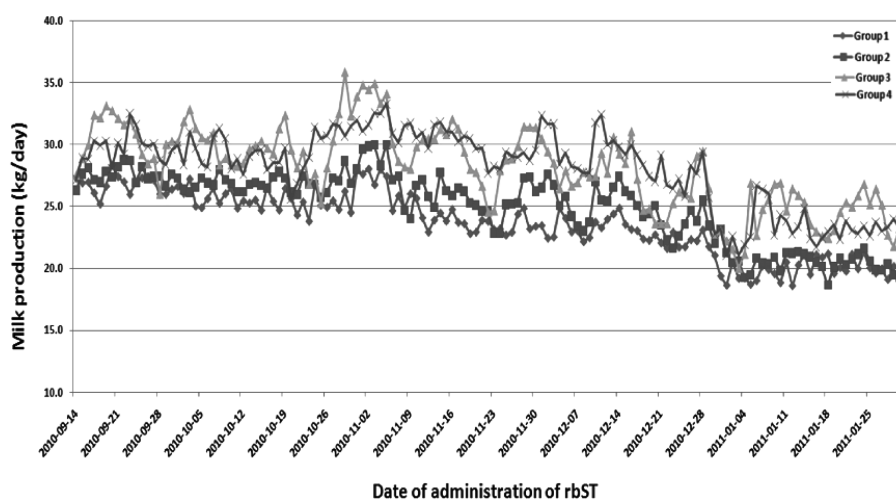


Fig 1. Milk production pattern of dairy cows which were administered rbST for 20 weeks. Control cows (Group I, \blacktriangle), Posilac[®] administered cows (Group II, \blacksquare), Boostin[®]-S administered cows (Group III, \blacktriangleleft), and Boostin[®]-250 administered cows (Group IV, \blacktriangleright).

Table 3. Changes of milk somatic cell count (\log_{10} SCC) in cows treated with rbST (Mean \pm SE)

Group	I	II	III	IV
1st week*	2.16 \pm 0.82	2.11 \pm 0.55	2.12 \pm 0.57	2.27 \pm 0.52
5th week	2.21 \pm 0.74	2.26 \pm 0.54	2.14 \pm 0.62	2.44 \pm 0.53
9th week	2.25 \pm 0.63	2.17 \pm 0.65	2.10 \pm 0.62	2.32 \pm 0.64
13th week	2.30 \pm 0.66	2.26 \pm 0.68	2.22 \pm 0.66	2.24 \pm 0.64

*Measurement were conducted at the time of each administration of rbST formulas.

Table 4. Changes of milk fat (%) in cows treated with rbST (Mean \pm SE)

Group	I	II	III	IV
1st week*	4.15 \pm 1.01	3.63 \pm 0.94	3.68 \pm 0.58	3.69 \pm 0.88
5th week	4.09 \pm 0.98	3.63 \pm 0.92	3.71 \pm 0.92	3.58 \pm 1.18
9th week	4.47 \pm 0.73	4.42 \pm 0.64	4.10 \pm 0.78	4.24 \pm 0.93
13th week	4.53 \pm 0.81	3.78 \pm 1.07	3.85 \pm 0.85	3.74 \pm 0.94

*Measurement were conducted at the time of each administration of rbST formulas.

Table 5. Changes of milk protein (%) in cows treated with rbST (Mean \pm SE)

Group	I	II	III	IV
1st week*	3.35 \pm 0.46	3.24 \pm 0.29	3.15 \pm 0.33	3.26 \pm 0.41
5th week	3.67 \pm 0.52	3.51 \pm 0.27	3.39 \pm 0.44	3.50 \pm 0.50
9th week	3.60 \pm 0.55	3.41 \pm 0.26	3.37 \pm 0.44	3.43 \pm 0.49
13th week	3.97 \pm 0.54	3.58 \pm 0.26	3.53 \pm 0.37	3.64 \pm 0.44

*Measurement were conducted at the time of each administration of rbST formulas.

imental period, outbreaks of clinical mastitis from Group I to Group IV) were 2, 3, 1, and 2 cases, respectively. The incidence of clinical mastitis (based on the number of cows treated) was not higher in rbST-supplemented groups than in control group (Table 2). Changes of milk SCC for cows supplemented with rbST during experimental period are presented on Table 3. Somatic cell count of each group fluctuated more or less during experimental period but there was no significant difference in values of \log_{10} SCC among supplementation groups.

Milk components

The means and standard errors of milk components from at the start of supplementation and 4 week intervals during the experimental period are shown from Table 4 to Table 6. In each group, there was a minor decrease of fat contents of milk during the first few weeks of rbST supplementation. These changes were considered by low consumption of dietic fibers which were required for increased milk production after rbST

Table 6. Changes of solid not fat (%) in cows treated with rbST (Mean \pm SE)

Group	I	II	III	IV
1st week*	8.68 \pm 0.33	8.67 \pm 0.32	8.58 \pm 0.27	8.68 \pm 0.31
5th week	9.05 \pm 0.29	9.01 \pm 0.27	8.96 \pm 0.38	9.02 \pm 0.30
9th week	8.96 \pm 0.50	8.91 \pm 0.36	8.93 \pm 0.57	8.98 \pm 0.53
13th week	9.29 \pm 0.44	9.08 \pm 0.34	9.07 \pm 0.34	9.18 \pm 0.37

* Measurement were conducted at the time of each administration of rbST formulas.

Table 7. Changes of body condition score in cows treated with rbST (Mean \pm SD)

Group	I	II	III	IV
1st week*	3.13 \pm 0.46	3.18 \pm 0.44	3.19 \pm 0.39	3.21 \pm 0.47
3rd week	3.11 \pm 0.49	3.15 \pm 0.43	3.07 \pm 0.45	3.11 \pm 0.56
5th week	3.13 \pm 0.46	3.07 \pm 0.47	3.06 \pm 0.44	3.11 \pm 0.57
7th week	3.15 \pm 0.46	3.05 \pm 0.49	3.00 \pm 0.42	3.08 \pm 0.52
9th week	3.17 \pm 0.48	3.06 \pm 0.46	2.97 \pm 0.41	3.07 \pm 0.52
11th week	3.20 \pm 0.43	3.03 \pm 0.52	2.97 \pm 0.42	3.05 \pm 0.55
13th week	3.23 \pm 0.43	3.06 \pm 0.53	3.00 \pm 0.41	3.09 \pm 0.56
15th week	3.22 \pm 0.46	3.03 \pm 0.55	3.02 \pm 0.46	3.09 \pm 0.55
17th week	3.25 \pm 0.47	3.08 \pm 0.55	3.05 \pm 0.42	3.17 \pm 0.58
19th week	3.29 \pm 0.46	3.11 \pm 0.55	3.07 \pm 0.43	3.17 \pm 0.60

*Measurement were conducted at the time of each administration of rbST formulas.

supplementation (Table 4 and 5). Fat and protein contents of milk were increased gradually until the end of experiment. Cows in negative energy balance produced lower content of milk protein. In each group, there was a minor change of solid not fat content of milk during the experiment (Table 6).

Body condition score (BCS)

Throughout the supplementation period, no significant differences in BCSs between the rbST supplementation groups and control group were observed (Table 7). The BCSs of control Group I were increased slightly during the experimental period. However, the BCSs of rbST supplementation groups were decreased slightly during the first 11 weeks of experiment. And the BCS of Group IV was decreased less than those of Group II and Group III during the experiment. Then BCSs of rbST supplementation groups increased gradually until the end of the experiment. The rbST supplementation to the dairy cows after the peak milk yield did not cause negative effect on BCS if cows had ingested adequate feed required for increased milk production. However, some cows less than 100 days in milking had decreased BCSs after rbST supplementation.

Discussion

The axiom of production animal agriculture is that the health and well being of domestic animals have direct and indirect relationships to their productive efficiency (11,12). High-producing dairy cows must be healthy to achieve sustained levels of above-average performance. The use of 500 mg of rbST every 2 weeks results in significant increases in milk production in dairy cows. However, it was concerned that the supplementation of rbST would induce metabolic stress in cows (4,17,18). This study was hypothesized that administration of 250 mg of rbST every week would be reduced metabolic stress of cows without negative effect on milk production. This study demonstrated comparable effects of rbST administration of 250 mg every week on milk yield and animal health with those of rbST administration of 500 mg every 2 weeks.

The cows receiving 500 mg of bST every 2 weeks were induced more milk yield than control cows from 3.1 kg/d (11.4%) to 3.7 kg/d (14.8%) (4,17,18). In this study, 500 mg of rbST treatments in every 2 weeks induced more milk yield than non-supplemented control from 2.9 kg/d (12.3%) to 4.2 kg/d (17.9%). And milk production in 250 mg of rbST supplemented cows in every week was similar to that of 500 mg of rbST supplemented cows every 2 weeks. The effect of rbST on the shape of the lactation curves were different depending on dose of rbST. In the pattern of milk production, fluctuation range of milk yield in cows of supplementation of 250 mg of rbST was lower than supplementation of 500 mg. As a result, supplementation of 250 mg of rbST every week can reduce metabolic stress in cows compared with supplementation of 500 mg of rbST every 2 weeks.

Clinical mastitis incidence was unaffected in cows supplemented with rbST in this study. The authors also reported that use of bST was not associated with clinical mastitis incidence (9,18,19). And there was no significant difference in values of \log_{10} SCC among treatment groups in this study. West *et al.* (22) reported Holstein cows exhibited a significant linear increase in SCC with increasing rbST dose. However, the other authors showed no effect of bST supplementation on milk SCC (4,8,19,20). Therefore, it was considered that rbST supplementation in this study did not affect the incidence of clinical mastitis and milk SCC. And the other disease was not observed throughout the experimental period.

In this study, fat contents of milk decreased slightly during the first few weeks of rbST supplementation and then fat contents increased gradually until the end of treatment. As the experiment started, protein contents of milk were low among all groups and cows with low BCS score produced lower protein content of milk. But after the addition of protein source, protein contents of milk were increased gradually until the end of experiment. Although there was a minor change of solid not fat content of milk during the experiment, it was not significant change. According to Bauman *et al.* (5), milk fat content of cows in positive energy balance is not influenced

by bST treatment and milk fat yield follows the trend of milk production. Administration of bST did not change milk protein percentage when cows were in positive nitrogen balance, but the milk protein percentage of cows in negative nitrogen balance tended to decline milk protein percentage (17-19,21). Bauman *et al.* (3) and Elvinger *et al.* (15) reported that rbST supplementation did no effect in solid not fat contents of milk.

BCSs of dairy cows were reduced in the first few weeks of rbST supplementation because of the immediate increase in milk yield with no concurrent increase in DMI (16). West *et al.* (24) reported that BCS during the rbST treatment study declined linearly with increasing bST dose. Chalupa *et al.* (7) also reported a significant reduction in body weight with increasing rbST dose. However, the other authors reported no change in body weight and BCS with rbST supplementation (3,5). In this study, decline in BCSs were similar among the rbST supplementation groups, but the BCS of no supplementation control group was slightly increased during the experimental period. Administration of 500 mg rbST to dairy cows every 2 weeks declined BCS during the first 11 weeks of experiment. And decline range of the BCS of 250 mg supplementation group was lower than those of 500 mg supplementation groups during the experiment. It was considered that supplementation of 250 mg of rbST every week can reduce the metabolic stress in cows compared with supplementation of 500 mg of rbST every 2 weeks. However, some cows less than 100 days in milking had declined BCSs after rbST supplementation. Therefore, the precise individual feeding management was necessary.

In conclusion, weekly administration of Boostin[®]-250 in dairy cows is alternative administration regimen which had same effect on milk production as Boostin[®]-S administration. The pattern of milk production in Boostin[®]-250 administered cows showed the lower range of fluctuation in milk production and it was speculated that the metabolic stress of dairy cows was alleviated. The rbST treatment in dairy cows did not affect on milk components, health status, and body condition score of cows. However, the weekly administration of Boostin[®]-250 required the double labor cost than biweekly administration of Boostin[®]-S.

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재조합 Bovine Somatotropin 250 mg 제제의 투여가 젖소의 산유량 및 건강에 미치는 영향

김요한 · 김 두¹

강원대학교 수의과대학 및 동물의학종합연구소

요 약 : 재조합 bST(recombinant bovine somatotropin; rbST)는 젖소에서 건강에 부작용을 초래하지 않으면서 유생산을 증가시키는 것으로 알려졌다. 본 연구는 250 mg의 rbST를 함유한 Boostin[®]-250 제제와 rbST를 500 mg 함유하는 Posilac[®]제제와 Boostin[®]-S 제제의 투여시 유생산에 미치는 영향과 대상동물에 대한 rbST 투여의 안전성을 비교하기 위하여 실시하였다. 젖소는 1군에서 4군까지 각각 25마리씩 임의배치하였다. Boostin[®]-250 제제와 부형제(대조군)를 매주 투여하였으며 Boostin[®]-S 제제와 Posilac[®]제제는 2주 간격으로 투여하였다. 젖소의 유량, 유성분, 체세포수, 건강상태, body condition score (BCS)를 측정하였다. Posilac[®]제제, Boostin[®]-S 제제, Boostin[®]-250 제제의 투여에 따른 유생산 증가는 대조군과 비교하여 각각 2.9 kg/day (12.3%), 4.2 kg/day (17.9%), 4.1 kg/day (17.4%)이었으며 rbST를 투여한 군들과 대조군 사이에서 통계적 유의차가 확인되었다. rbST의 투여는 임상형 유방염발생과 우유의 체세포수를 증가시키지 않았으며 rbST의 투여는 유성분에도 큰 영향을 미치지 않았다. 최고유량 이후 rbST의 투여는 BCS에 부정적인 영향을 미치지 않았지만 비유 100일 이내의 일부 젖소들은 rbST의 투여 후 BCS가 감소하였다. 결론적으로 rbST 250 mg의 매주 투여는 rbST 500 mg의 2주 간격 투여와 유사한 우유 증산효과를 나타내었으며 젖소의 대사성 스트레스를 감소시키는 것으로 판단되었다.

주요어 : rbST, 250 mg, 젖소, 유생산, 건강