

## EFFECTS OF BOVINE SOMATOTROPIN ON THE PATTERN OF MILK YIELD WITHIN AND BETWEEN INJECTION INTERVALS IN WEST AFRICAN DWARF GOATS

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### ABSTRACT

Twenty-four West African Dwarf (WAD) goats were used to study the pattern of milk yield response to recombinant bovine somatotropin (rbST) administered in a sustained-delivery vehicle. The goats were divided equally into four treatment groups, each comprising of six does. The first group (control, T<sub>0</sub>) received no rbST while the other groups received rbST (T<sub>1</sub>, 20 mg; T<sub>2</sub>, 40 mg; T<sub>3</sub>, 60 mg) injected at 2-week intervals commencing from the 7<sup>th</sup> week postpartum for 6 weeks. Pattern of milk yield response to rbST was significantly (p<0.05) influenced by rbST dose, day from rbST treatment, order of rbST treatment and parity. Milk yield of treated goats increased from day 1 of treatment, peaked between day 5 and day 8 after treatment and progressively decreased until day 14 of treatment but that of the control decreased progressively from day 1 till day 14 of treatment. The mean relative response of DMY to rbST treatment for T<sub>1</sub>, T<sub>2</sub> and T<sub>3</sub> exceeded T<sub>0</sub> by 50.36, 68.00 and 71.16 % respectively and significantly affected the shape of the lactation curve, thus, improving persistency of lactation. The patterns of DMY for T<sub>1</sub>, T<sub>2</sub> and T<sub>3</sub> were well-fitted by the Wood's equations;  $Y = 16.628n^{1.728}e^{-0.439n}$  (R<sup>2</sup> = 63.1),  $Y = 25.198n^{0.836}e^{-0.239n}$  (R<sup>2</sup> = 75.6) and  $Y = 0.008n^{9.081}e^{-1.352n}$  (R<sup>2</sup> = 42.3) respectively. The administration of 40 mg dose of rbST appears to elicit DMY response that favoured milk yield persistency. But since highest DMY was observed with 60 mg dose of rbST, estimation of optimal dose that would elicit maximum DMY response may be required in order to validate the statement. Our findings suggest that rbST administration to WAD goats after peak of lactation can enhance milk yield, galactopoiesis and persistency of lactation indicating higher milk yield in extended lactation.

**Key words:** WAD goats, milk yield, recombinant bovine somatotropin, Wood's equation.

### INTRODUCTION

The administration of exogenous recombinant bovine somatotropin (rbST) is an efficient biotechnological tool used to improve the performance of cattle including efficient milk production. Its effects on milk yield and composition in dairy cows have been

reviewed extensively (Bauman, 1992; Gallo *et al.*, 1997; Etherton and Bauman, 1998). The primary effect of rbST administration in a sustained-delivery vehicle on dairy cows is the provision of its galactopoietic capacity that alters the shape of the lactation curve, which exhibits cyclical pattern of milk yield

between two consecutive injections (Hartnell *et al.*, 1995; Kim *et al.*, 1991; Schams *et al.*, 1991) resulting in improved lactation persistency (Peel and Bauman, 1987; Chilliard, 1989; Bauman, 1992). Baldi *et al.* (2002) reported that milk yield response to the third injection of rbST was greater (+60% compared with the controls) than to the second (+46%) and the first (+31%) injections; thus, rbST affected the shape of the lactation curve. Gallo *et al.* (1997) asserted that this response was a medium term effect of rbST treatment, which improved lactation persistency. Information about the use of rbST for increased milk yield in West African Dwarf (WAD) goats is much scarcer than in temperate dairy goats where about 5 – 30% increase in milk yield has been reported (Disenhaus *et al.*, 1995). Moreso, knowledge of the effects of rbST administration on the shape and persistency of the lactation curve in WAD goats is lacking. Therefore, there is need to study the effects of rbST administered in a sustained-delivery vehicle on milk yield and pattern of response of WAD goats to consecutive injections of exogenous rbST.

## **MATERIALS AND METHODS**

### ***Description of experimental site***

The experiment was conducted at the Goat Unit of the Teaching and Research Farm of the College of Animal Science and Livestock Production, University of Agriculture, Abeokuta. Abeokuta falls within the Rain Forest Vegetation zone of South-Western Nigeria at latitude 7°13' 49.46"N, longitude 3°26' 11.98"E (Google Earth, 2006) and

altitude of 76 meters above sea level. The climate is humid with a mean annual rainfall of 1037 mm. The annual mean temperature and humidity are 34.7°C and 82% respectively.

### ***Animals and management***

Twenty-four lactating West African Dwarf does (12 primiparous and 12 multiparous) whose body weights (BW) ranged from 11-16 kg selected from the existing flock on the farm were used for the study. The goats were under intensive management system with zero grazing ('cut and feed') and were housed individually in cross-ventilated pens with slated floors. Water was given *ad libitum*, 0.5 kg/head/day of concentrate feed supplement and 1.0 kg/head/day chopped *Panicum maximum* grass were offered to the goats. The proximate compositions of the concentrate feed and the grass are shown in Tables 1 and 2 respectively.

### ***Experimental procedure***

Based on daily milk yield from kidding, BW and days in milk (DIM) prior to rbST treatment, pre-treatment milk yields were obtained and are given in Table 3. The does were assigned into four treatment groups, each group comprising of six does with first and second parity evenly distributed as well as liveweight equalization among treatment groups.

**Table 1: Chemical composition of feed supplement fed to lactating West African Dwarf does**

Ingredients	% Composition
Maize	10.00
Wheat offal	40.00
Brewers dried grain	30.00
Palm kernel cake	18.00
Bone meal	1.00
Salt	1.00
Total	100.00
Crude protein	17.44
Crude fibre	11.56
Ether extract	4.68
Metabolizable energy (kcal/kg)	2076.70

**Table 2: Chemical composition of *Panicum maximum* grass fed to lactating West African Dwarf does**

Proximate component	% Composition
Crude protein	5.37
Crude fibre	33.35
Neutral detergent fibre	66.31
Acid detergent fibre	42.79
Acid detergent lignin	19.71

**Table 3: Group size, BW, daily milk yield, and DIM prior to rbST treatment in West African Dwarf goats during lactation**

	Treatment group			
	bST dose			
	0 mg	20 mg	40 mg	60 mg
No. of goats	6	6	6	6
No. of primiparous does	3	3	3	3
No. of second parity does	3	3	3	3
BW,1 kg	15.27	15.05	15.10	15.03
Milk yield,1 ml/day	149.26	148.90	149.01	150.10
DIM <sup>1</sup>	50	49	50	49

<sup>1</sup>Means of treatment groups did not differ significantly ( $p>0.05$ )

BW = Body weight and DIM = Days in milk

The first group, which was the control (T<sub>0</sub>) received no bovine somatotropin injection while the remaining three groups received bovine somatotropin injections at different doses: 20 mg (T<sub>1</sub>), 40 mg (T<sub>2</sub>) and 60 mg (T<sub>3</sub>). The bovine somatotropin, Lactotropina<sup>MR</sup>, division Sanidad Animal, Eli Lilly CO., Mexico is in a sustained-release vehicle formulation for 14 days interval. The bovine somatotropin doses were administered subcutaneously at the left and right scapular regions (Davis *et al.*, 1999) alternately every 14 days commencing from 7<sup>th</sup> to 11<sup>th</sup> week of lactation with a total of 3 injections per doe. The doses were selected based on the preliminary results obtained by Rekwot (personal communication) on the study on milk yield and composition of Red Sokoto goats, administered bovine somatotropin at the National Animal Production Research Institute (NAPRI), Nigeria. The study on the effect of recombinant bovine somatotropin (rbST) administration on milk production, composition and some haemato-biochemical parameters of lactating goats in Egypt, by Sallam *et al.* (2005) also provided basis for the selection of the doses. The does were milked twice daily at 7:30 a.m. and 7:30 p.m. for 42 days commencing from the 7<sup>th</sup> to the 12<sup>th</sup> week of lactation. The a.m. and p.m. yields were added to determine the daily milk yield and individual milk yield was recorded daily.

**Computation and statistical analysis**

The data on daily milk yield (DMY) was analysed with respect to two time-dependent variables comprising: 1. Days from rbST administration ranging from 1 (the day of actual or sham injection for treated and control goats, respectively) to 14 (day before the subsequent actual or sham injection), and 2. Order of injection (O), ranging from 1 to 3 for both treated

and control goats. The least squares procedure of Systat Analytical Computer Package, version 5.02 (SYSTAT, 1992) was used to perform Analysis of Variance (ANOVA) for data involving repeated measurements over time according to the following statistical model:

$$Y_{ijklm} = \mu + T_i + D_j + O_k + P_l + T^*D_{ij} + T^*O_{ik} + T^*P_{il} + \epsilon_{ijklm}$$

where:

- Y<sub>ijklm</sub> = Trait of interest
- T<sub>i</sub> = Fixed effect of i<sup>th</sup> rbST dose (i = 1-4)
- D<sub>j</sub> = Fixed effect of j<sup>th</sup> days from rbST treatment (j = 1-14)
- O<sub>k</sub> = Fixed effect of k<sup>th</sup> order of rbST treatment (k = 1-3)
- P<sub>l</sub> = Fixed effect of l<sup>th</sup> parity (k = 1-2)
- T\*D<sub>ij</sub> = The interaction between i<sup>th</sup> rbST dose and j<sup>th</sup> days from rbST treatment
- T\*O<sub>ik</sub> = The interaction between i<sup>th</sup> rbST dose and k<sup>th</sup> order of rbST treatment
- T\*P<sub>il</sub> = The interaction between i<sup>th</sup> rbST dose and l<sup>th</sup> parity of does.
- ε<sub>ijklm</sub> = Random error associated with each record.

The least squares means of interaction of rbST dose and days from rbST treatment of treated goats were used to study a model that was able to describe the change of milk yield following an administration of rbST injection.

The relative response of DMY to rbST doses within injection interval of WAD does was computed as a deviation of least squares means of milk yield at day i (i = 1,...,13) of the injection interval from least squares means of milk yield at 14<sup>th</sup> day of the injec-

tion interval (Gallo *et al.*, 1997). The pattern and relative response of DMY to rbST doses within injection interval were also fitted by Wood's equation (Wood, 1967). The equation is:

$$Y = An^{be-cn}$$

Where:

- Y = Relative response of DMY to rbST treatment  
 A = General level of relative response of DMY to rbST treatment  
 b = Rate of increase of relative response of DMY before peak  
 c = Rate of decrease of relative response of DMY after peak  
 n = Days from rbST treatment  
 (A, b and c are constant terms which represent response rate parameters)

The response rate parameters were estimated using the non-linear (NONLIN) regression Procedure of Systat Analytical Computer Package, version 5.02 (SYSTAT, 1992).

The rate of decline and persistency of milk yield of rbST-treated goats and control were determined by relative changes of daily milk yield in percentages between the three order of rbST treatments (7-12<sup>th</sup> week of lactation) as computed by Gallo *et al.* (1997). The mean difference in daily milk yield between control and rbST-treated goats (i.e. response to rbST) was also computed in order to explain persistency of lactation.

## RESULTS AND DISCUSSION

The summary of least squares analysis of variance on the effects of rbST dose, day from rbST treatment, order of rbST injection and parity on daily milk yield (DMY) is presented in Table 4. DMY was signifi-

cantly ( $p < 0.001$ ) influenced by bST dose, order of injection and parity. There were no significant ( $p > 0.05$ ) interactions between rbST dose and day from rbST treatment and rbST dose and order of rbST treatment. DMY during the entire period of rbST treatment of does increased significantly ( $p < 0.001$ ) with increased levels of bST doses with mean values of 140.04, 210.57, 235.27 and 239.69 ml for T<sub>0</sub> (0mg), T<sub>1</sub>, T<sub>2</sub> and T<sub>3</sub> respectively. The mean DMY of T<sub>1</sub>, T<sub>2</sub> and T<sub>3</sub> exceeded T<sub>0</sub> by 50.36, 68.00 and 71.16% respectively.

There is difficulty in comparing the result of this present study with other studies because reports related to administration of exogenous somatotropin in goats are scarce, more so in the West African Dwarf breed of goats that have not been selected for dairying. Protocols for treatment are not always comparable among trials and results obtained are not consistent. Jammes *et al.* (1996) reported that administration of bST to lactating goats increased milk production by 50 – 60 %. The finding was close to the observation made in this study. Chadio *et al.* (2000) administered 160 mg of a sustained-release formulation of rbST to cross bred Alpine goats for 84 days through bi-weekly injections and observed an increased milk yield (nearly 13%) compared with the untreated group. Conversely, Baldi *et al.* (2002) found a higher increase of 20% in daily milk yield after Saanen goats received 120 mg per 2 weeks of slow-release rbST for 42 days. The galactopoietic capacity of rbST in the present study seems to be higher than the one observed in sheep (45 – 55 %; Fernandez *et al.*, 1995; Chiofalo *et al.*, 1999) and in cows (15 – 25 %; Bauman and Vernon, 1993). The disparity could be attributed to differences in species of animals used and different stages of lactation when rbST was administered. While different biological potencies of the rbST preparations may ac-

count for some differences in biological effects, an alternative explanation may be related to the fact that the WAD goats used in this study had not undergone the same extensive selection for high milk production as did dairy sheep and cows. Thus the high response of milk yield to bST in WAD does may reflect the difference between the actual levels of production and physiological potentials for milk production.

Parity of does highly affected DMY, and as expected, the 2<sup>nd</sup> parity does had higher DMY than the 1<sup>st</sup> parity does with mean

values of 165.73 vs. 114.36ml/day, 249.88 vs. 171.25ml/day, 257.41 vs. 213.13ml/day, 260.18 vs. 219.21 for T<sub>0</sub>, T<sub>1</sub>, T<sub>2</sub> and T<sub>3</sub> respectively. The observation could be attributed to larger udder size with larger population of milk secreting cells (alveoli) available for higher milk synthesis and secretion. Since udder size is positively correlated with milk yield (James, 2000). Bemji *et al.* (2007) made similar observations in WAD and Red Sokoto goats in Nigeria. There was significant (p<0.001) interaction between rbST treatment and parity.

**Table 4: Summary of least squares analysis of variance showing the effects of bovine somatotropin (rbST) dose, day from rbST treatment, order of rbST treatment and parity on daily milk yield of West African Dwarf goats during combined entire period of bST treatment**

Source of variation	DF	Mean-Square
		Daily milk yield
rbST treatment (D)	3	534454.58***
Day from rbST treatment (T)	13	7588.84***
Order of rbST treatment (O)	2	32367.14***
	1	729737.86***
Parity (P)	39	578.80
D × T	6	4431.18
D × O	3	18425.63***
D × P	940	2135.80
Error		

\*\*\*p<0.001

In T<sub>0</sub>, DMY within injection interval of does decreased insignificantly ( $p > 0.05$ ) from 154.47 ml on the 1<sup>st</sup> day of injection to 136.25 ml on the 14<sup>th</sup> day of injection. In T<sub>1</sub>, it increased from 214.33 ml on the 1<sup>st</sup> day of injection to 231.47 ml on the 7<sup>th</sup> day of injection and then after decreased to 194.44 ml on the 14<sup>th</sup> day of injection. In T<sub>2</sub>, it increased from 238.89 ml on the 1<sup>st</sup> day of injection to 245.56 ml on the 5<sup>th</sup> day of injection and then after decreased to 215.06 ml on the 14<sup>th</sup> day of injection. In T<sub>3</sub>, it increased from 246.89 ml on the 1<sup>st</sup> day of injection to 255.39 ml on the 8<sup>th</sup> day of injection and then after decreased to 226.17 ml on the 14<sup>th</sup> day of injection (Figure 1).

The consistent decrease in DMY of WAD does not treated with rbST from 1<sup>st</sup> – 14<sup>th</sup> day of rbST treatment and persistent increase in DMY of WAD does treated with rbST up to 5<sup>th</sup> – 8<sup>th</sup> day of treatment before decreasing up to 14<sup>th</sup> day of rbST treatment observed showed that WAD does treated with bST exhibited persistency of lactation more than does in the control. The progressive decrease in DMY of does in the control group from 1<sup>st</sup> – 14<sup>th</sup> day of rbST treatment is a normal physiological process in lactation because goats were in their declining phase of lactation when milk secreting tissue rapidly begins to regress. The observation made on goats treated with rbST could be due to the galactopoietic activity of rbST and ability to enhance proliferation, maintain and stimulate activity of the milk secreting cells (alveoli).

This observation contradicts in part, the report of Gallo *et al.* (1997) that DMY of Alpine does increased from 1<sup>st</sup> day of injection, peaked between 3<sup>rd</sup> – 5<sup>th</sup> day after administration, and then decreased progressively until the following injection. The dis-

parity could be attributed to differences in breed, stage of lactation when rbST treatment commenced, type, dosage and formulations of rbST and largely to the degree of genetic selection for dairy production. In this study, WAD goats, which has not been selected and developed for dairying as against Alpine goat breed, which has been extensively selected for dairy production, were used. On the same vein, bST (Lactotropina<sup>MR</sup>; 20 mg – 60 mg per 2 weeks) was administered vis-à-vis Somodobove; 90 mg per 4 weeks at 7<sup>th</sup> week of lactation as demonstrated by Gallo *et al.* (1997).

In T<sub>0</sub>, DMY between injection intervals of does decreased significantly ( $p < 0.001$ ) from 149.84 ml with the 1<sup>st</sup> injection at 7<sup>th</sup> week of lactation to 140.41 ml with the 2<sup>nd</sup> injection at 9<sup>th</sup> week of lactation and then after to 129.88 ml with the last injection at 11<sup>th</sup> week of lactation. In T<sub>1</sub>, it decreased significantly ( $p < 0.001$ ) from 221.18 ml with the 1<sup>st</sup> injection at 7<sup>th</sup> week of lactation to 218.01 ml with the 2<sup>nd</sup> injection at 9<sup>th</sup> week of lactation and then after to 192.52 ml with the last injection at 11<sup>th</sup> week of lactation. In T<sub>2</sub>, it increased significantly ( $p < 0.001$ ) from 236.17 ml with the 1<sup>st</sup> injection at 7<sup>th</sup> week of lactation to 239.61 ml with the 2<sup>nd</sup> injection at 9<sup>th</sup> week of lactation and then after decreased to 230.02 ml with the last injection at 11<sup>th</sup> week of lactation. In T<sub>3</sub>, it decreased significantly ( $p < 0.001$ ) from 254.89 ml with the 1<sup>st</sup> injection at 7<sup>th</sup> week of lactation to 254.89 ml with the 2<sup>nd</sup> injection at 9<sup>th</sup> week of lactation and then after to 231.62 ml with the last injection at 11<sup>th</sup> week of lactation. The consistent decrease in DMY observed between 1<sup>st</sup> and last injections in T<sub>0</sub>, T<sub>1</sub> and T<sub>3</sub> respectively clearly indicated that 0, 20 and 60 mg doses of rbST could not substantially elicit persistency in DMY whereas the increase in DMY from 1<sup>st</sup> to 2<sup>nd</sup> injections before decreasing at

last injection showed that 40 mg dose of rbST was able to elicit DMY response that favoured milk yield persistency. But since highest DMY was observed with 60 mg dose of rbST, estimation of optimal dose that would elicit optimal DMY response may be required in order to validate the statement.

Immediate DMY response to rbST treatment has been described for dairy cows (Gallo *et al.*, 1994) through a third-order polynomial regression function, but the coefficients obtained were meaningless for biological application. In this study, Wood's equation was used to model the immediate response to rbST, which fitted-well the pattern of DMY change and generated parameters of biological meaning. To this end, milk yield by day within the mean injection for different doses of rbST for treated goats has been expressed as a relative response of DMY (Figure 2) and computed as deviation of least squares means of milk yield at day 1 to day 13 of the treatment interval from least squares means of milk yield at day 14 of the treatment interval. As shown in Figure 2, relative response of DMY was fitted by Wood's equation explained a large part of the changes observed ( $R^2 = 42 - 76\%$ ). Parameters generated by the function described the kinetics of DMY response to rbST administration. Parameter A in the function is a constant that can be interpreted as the theoretical daily milk yield response to the exogenous hormone with the hypothesis that rbST was entirely and immediately available after injection; the values for parameter A in T<sub>1</sub>, T<sub>2</sub> and T<sub>3</sub> were 16.63, 25.20 and 0.01 ml/day respectively. This clearly shows that administration of 40 mg dose of rbST produced the highest relative response of DMY. The dose is lower than 50 mg per 2 weeks observed by Rek-

wot (personal communication) in his preliminary findings on Red Sokoto goats at National Animal Production Research Institute of Nigeria. The differences could be attributed to differences in breed of animal used. The b and c were rate constants; b expressed the rate of gain in response, which was the rate of increase of DMY immediately after injection and c expressed the rate of loss of response, which indicated the rate of decrease of DMY that occurred after the peak.

The relative rate of increase of DMY immediately after injection (i.e. before the peak) was significantly ( $p < 0.001$ ) higher in T<sub>3</sub> (9.08 ml/day,  $R^2 = 42.3$ ) than in T<sub>1</sub> (1.73 ml/day,  $R^2 = 63.1$ ) and T<sub>2</sub> (0.84 ml/day,  $R^2 = 75.6$ ) but the relative rate of decrease of DMY after the peak was significantly ( $p < 0.001$ ) lower in T<sub>2</sub> (-0.24 ml/day,  $R^2 = 75.6$ ) than in T<sub>1</sub> (-0.44 ml/day,  $R^2 = 63.1$ ) and T<sub>3</sub> (-1.35 ml/day,  $R^2 = 42.3$ ). Negative responses of DMY to rbST injections were observed around 12<sup>th</sup> day of treatment in T<sub>1</sub> and T<sub>3</sub> respectively and positive response of DMY to rbST injections within 14<sup>th</sup> day of rbST treatment was observed in T<sub>2</sub> (Figure 2). This indicated that T<sub>2</sub> (40 mg dose of rbST) exhibited consistent superiority in maintaining persistency of lactation than for other treatment groups. Nevertheless, estimation of optimal dose that would elicit optimal DMY response may be required in order to validate the statement.

The shape of the response curve should probably reflect the amount of rbST that was available for tissues. Schams *et al.* (1991) and Gallo *et al.* (1997) found nearly identical pattern for milk yield after administration of recombinant bovine somatotropin (rbST) at 2 weeks and 4 weeks injection intervals respectively in a sustained-delivery vehicle. It can be hypothesized that the b parameter



could have reflected the activation of bST from the vehicle and the biological effects on the body organs, whereas c parameter could have indicated the rate of decrease in the release from the vehicle and the rate of metabolic clearance of the exogenous hormone. However, because of the lack of data on plasma somatotropin and the somatomedins (IGF-I and IGF-II) content, this comment needs direct validation.

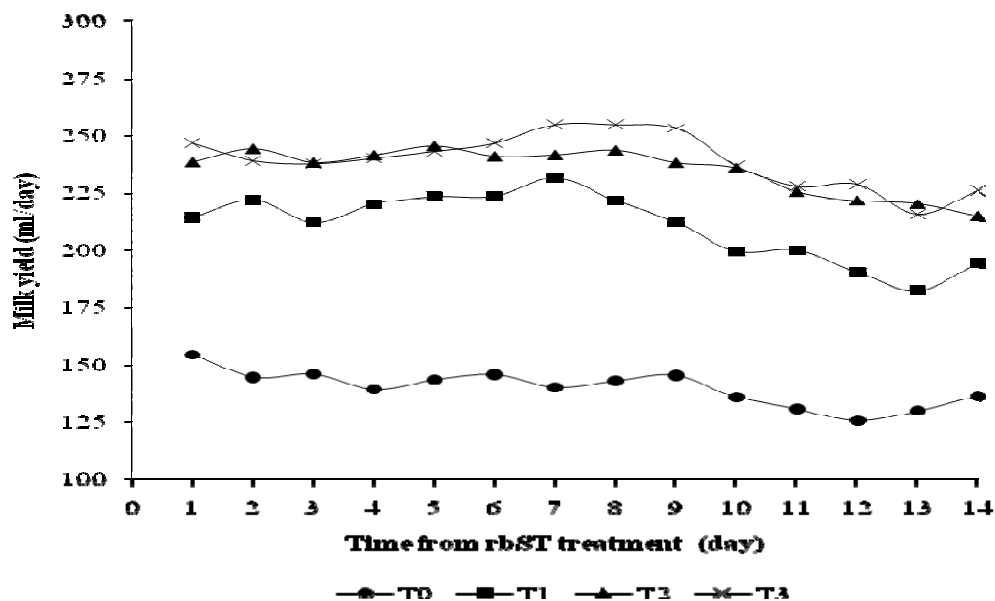


Figure 1: Pattern of daily milk yield within injection interval for goats not treated with rbST (T<sub>0</sub>), goats treated with 20 mg rbST (T<sub>1</sub>), 40 mg rbST (T<sub>2</sub>) and 60 mg rbST (T<sub>3</sub>). Values represent the means across three treatment intervals

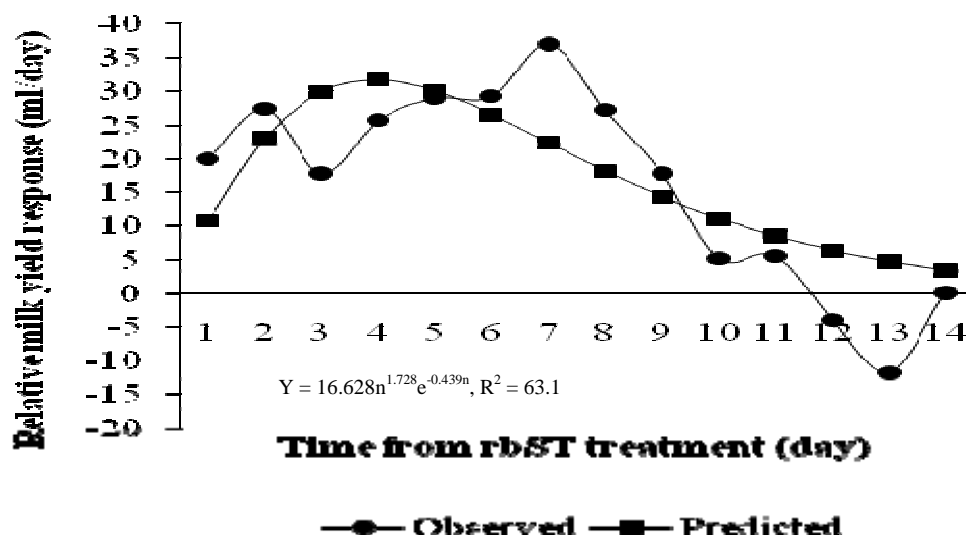


Figure 2a: Trend of observed and predicted pattern of relative milk yield response within injection interval for goats injected with 20mg (T<sub>1</sub>) of rbST

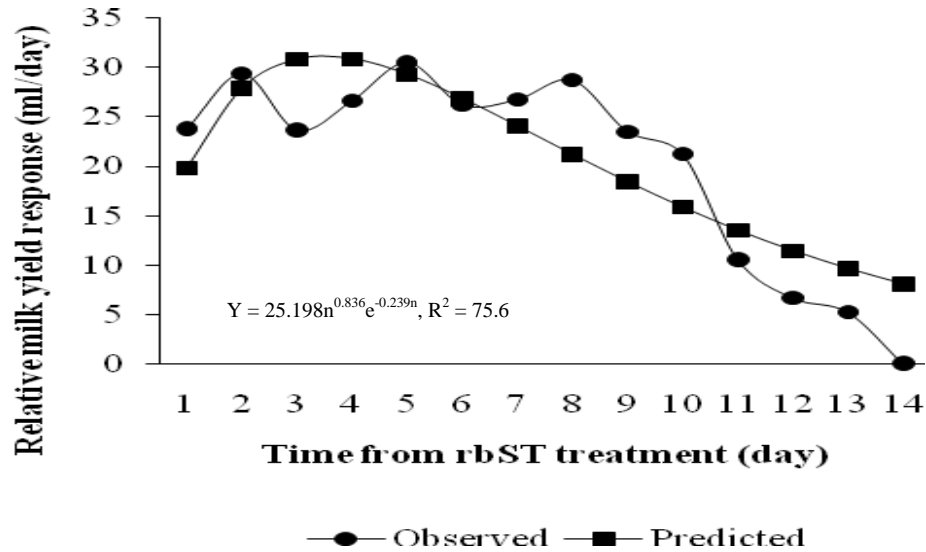


Figure 2b: Trend of observed and predicted pattern of relative milk yield response within injection interval for goats injected with 40mg (T<sub>2</sub>) of rbST

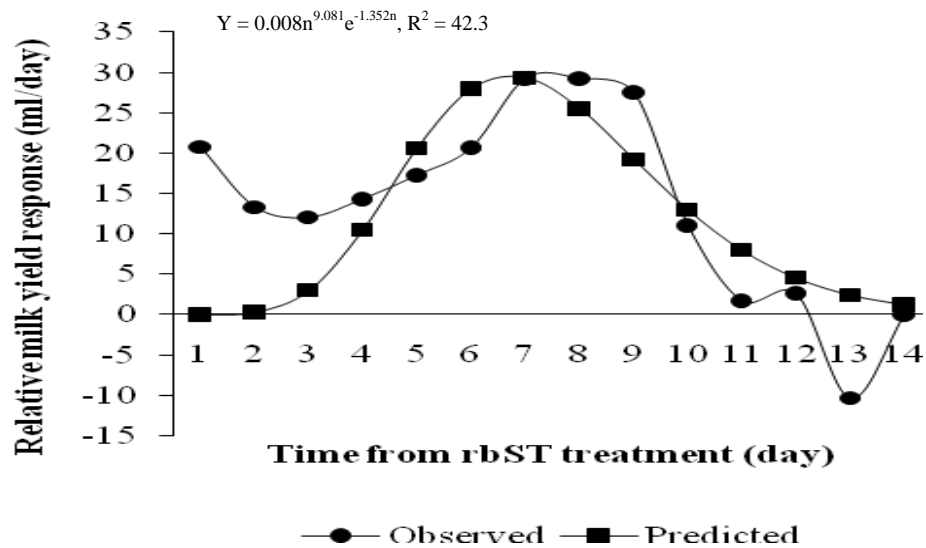


Figure 2c: Trend of observed and predicted pattern of relative milk yield response within injection interval for goats injected with 60mg (T<sub>3</sub>) of rbST

Figure 2: Trend of observed and predicted pattern of relative milk yield response within injection interval for goats not injected with bST (control, T<sub>0</sub>), group injected with 20mg bST (T<sub>1</sub>), 40mg bST (T<sub>2</sub>) and 60mg bST (T<sub>3</sub>)

**CONCLUSION**

The administration of bovine somatotropin (bST) (Lactotropina<sup>MR</sup>) in a slow-release formulation to lactating West African Dwarf (WAD) goats after peak of lactation increased milk yield over the entire period of rbST treatment by 50 – 71 % over the control and significantly affected the shape of the lactation curve, thus, improving persistency of lactation. Milk yield of WAD does treated with rbST increased from the 1<sup>st</sup> day of treatment, peaked between 5<sup>th</sup> – 8<sup>th</sup> day of treatment and progressively decreased until the 14<sup>th</sup> day of treatment but that of the control decreased progressively from the 1<sup>st</sup> day till the 14<sup>th</sup> day of treatment. The pattern of relative response of DMY to rbST treatment was well-fitted by the Wood's equation. The administration of 40 mg of rbST appears to be the dose that was able to elicit DMY response that favoured milk yield persistency. But since highest DMY was observed with 60 mg dose of rbST, estimation of optimal dose that would elicit optimal DMY response may be required in order to validate the statement.

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