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REVIEW ON THE ROLE OF BOVINE SOMATOTROPIN HORMONE FOR DAIRYING

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Supporting Information

REVIEW
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ABSTRACT: Bovine somatotropin (bST) is a metabolic protein hormone used to increase milk production in dairy cows. This hormone is important for growth, development, and other bodily functions of all animals. The only source of bST is from the pituitary glands of slaughtered cattle. Dairy cows are usually injected subcutaneously the volume of injective of a commonly used formulation is 1.4ml. The injection is typically repeated every 14 days. BST has the potential to increase the efficiency of milk production but there is no a change in milk composition. Potentially 10-15% more milk can be obtained from each cow with a cost of implementation of less than 5%. Good management measures recommended by a product manufacturer to ensure a high response in milk yield to bST administration. It increases the body weight and heat stress of the user animals. However, culling rate is higher in the bST treated animals than the non-treated. This hormone also does not have side effect on the health of human being (it is a treatment of children suffering from hypopituitary dwarfism as well as animas, but it increases the frequency of certain disease conditions such as mastitis and foot problems in cows. Therefore, using bST hormone is an important for developing countries which is food insecure and poor productive dairy cow, because even if it costs and needs good management, will not have said effect on human being, animals as well as environment.

Keywords: Bovine somatotropin hormone, Dairy, Effect, Milk

INTRODUCTION

There is a rapid increase in the human population particularly in developing countries. The demand and supply gap for food is increasing with time. To narrow this gap, multi-dimensional approaches are being carried out. Proponents of a new type of technology biotechnology claim that it will supply more food at less cost to meet this growing demand. One of the major agriculture related products of biotechnology research is bovine somatotropin (bST) (Jabbar et al., 2009). Naturally produced by a cow's pituitary gland, bST is one of the hormones involved in normal growth, development of mammary gland and normal milk production (Murphy, 1998). Bovine somatotropin (bST) is naturally occurring protein produced by the pituitary gland in all cattle. Recombinant bovine somatotropins (rbST), which differ from their native form by several amino acids, have been synthesized and manufactured using recombinant DNA techniques to increase milk production in dairy cows. The Food and Drug Administration (FDA) approved rbST product in 1993 after determining that its use would be safe and effective (Soliman, 2014).

It is a metabolic hormone, not a growth hormone like a steroid, which is released from the anterior pituitary gland of cattle and, until recent years, could be produced only by cows (Kohout et al., 2008). Bovine somatotropin (bST) increases milk production in dairy animals. The maximum increase in milk production has been observed up to 41%. Somatotropin did not change milk composition significantly. During short-term application of bST, cows mobilized their body reserves to support the increased milk production. Although DM intake of cows was increased in the long term applications, however, gross efficiency of production was improved due to larger increase in milk production than DM intake. Repartitioning of nutrients in body-tissue was primarily responsible for the increase in milk-production but defining the exact mechanism by which bST exerted its effect still (Sarwar and Tanveer, 2002).

There is no question that bST use increases milk yield and production efficiency. However, there are many factors that affect the magnitude of the milk production response, and study results vary widely. A number of factors have been identified as influencing milk production response in bST research trials: the quality of herd management, including the availability and quality of feed; the dosage of bST; when bST is administered during a cow's lactation, with the largest increases in milk production occurring when bST is administered following the peak

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in the lactation cycle, 63-90 days following calving; the age of the cow, with first lactation cows having a lower response than older cows; and the body condition of the cow prior to the start of treatment, and the cow's initial health before and during treatment (Kohout, 2008).

The genes responsible for production of bST in cattle were identified in bovine tissue cells; they cause the pituitary cells to produce the biological product bST. These genes were isolated and inserted into specific bacteria as part of a plasmid, with gene splicing. As these altered bacteria replicate, the new genes are also replicated and passed along to all new bacteria. The presence of these genes causes the bacterial cell to become a little "manufacturing plant" which produces bST in large quantities. Eventually the bacterial cells are killed and removed, leaving the purified bST. Based on the above facts the main objective of this paper is to review the effect of bovine somatotrophine hormone on dairying cows.

Sources and how to use bST

Commercially produced bST is very similar to naturally occurring bST found in the bovine Pituitary, with only a single amino acid difference or a few amino acid differences according to the manufacturers. Originally, the only source of bovine growth hormone was the pituitary gland of dead cattle. This method, however, produced very little of the hormone. Since those days a process was developed to mass produce bovine growth hormone in amounts previously impossible. Scientists, after determining which gene controls production of bovine growth hormone, were able to insert the gene into the Escherichia coli bacteria (E. coli). This method allowed for larger scale production of bovine growth hormone in a laboratory setting.

Dairy cows are usually injected subcutaneously in the ischiorectal fossa (depression beside the tail head) or behind the shoulder (post scapular). The volume of injective of a commonly used formulation in the U.S.A. is 1.4ml. The injection is typically repeated every 14 days. Feeding bST to cows will not work. Amino acids and peptides are the building blocks of proteins. The hormone bST is a complex protein that is immediately broken down into small, inactive amino acids and peptides and rendered ineffective when it enters a cow's digestive system. How often a cow must be injected with bST will depend on whether a bST product can be developed that releases the hormone gradually over a long period of time.

BST has been used to increase milk production; in this case bST is given from the ninth or tenth week after calving until the end of lactation. In the US the generally claimed responses are from 2.25 litters to 6.6 litter of milk/cow/day (Davis et al., 1988). To extend the lactation of cows that would otherwise be culled because of inability to breed or other health reasons. BST can be used to keep a cow in production for 30 to 100 days extra. The exact details of how bST increases milk production are not known, but it is thought that blood flow to the cows' mammary (milk-producing) gland is increased. The blood carries an increased amount of nutrients available for milk production. More nutrients are extracted from the blood by the mammary gland, which improves efficiency of milk production. Feed efficiency (pounds of milk produced per pound of feed consumed) is improved because more milk is produced and the proportion of feed used for body maintenance is decreased. The actual amount of feed consumed by bST treated cows' increases, helping the cow meet the increased nutrient demands.

Management factors and the use of bST

Quality of management is a major factor determining milk yield response as is the quantity and quality of feed provided. Good management measures recommended by a product manufacturer to ensure a high response in milk yield to bST administration include; cows should not be overcrowded, additional ventilation or cooling systems may be needed if not adequate, flooring should be kept clean and provide adequate traction, feeding areas should be designed to facilitate feeding, adequate water must be provided, cows should be protected from the effects of heat in hot weather and adequate shade should be provided, high quality feed should be available, fly control is imperative (Rock et al., 1989).

It is evident that such measures would improve cow welfare. However, use of bST in the absence of such measures would exacerbate welfare problems. It has been suggested that, if there are adverse effects in cows treated with bST, the farmers are not managing their animals well enough. Hence farmers who do find that their cows have mastitis, foot disorders, reproductive disorders or other problems specified as a potential risk when bovine somatotropin is used may be reluctant to report the occurrences. Any failure of farmers to report problems would affect the results of follow up studies after bST use.

Effect of bST on dairy cow and human health

Milk yield

According to the reviewed paper of Sarwar and Tanveer (2002) effect of bovine somatotropin on the lactational and reproductive performance of lactating dairy cows. Daily administration of exogenous bST derived from the extracts of pituitary glands, or even the growth hormone release factor from the extracts of the hypothalamus of slaughtered cows (Enright et al., 1988) or recombinantly derived bST, cause a higher milk-yield without altering the gross composition. Official estimates of the yield response to bST administration have varied from 10-25% (AHI, 1987) to 10-15% (CAST, 1993). However, responses can be variable and may depend on management factors to achieve a maximal response.

In a long-term study with Holstein cows, bST treatment increased the average fat-corrected milk (FCM) yield in a dose- dependent fashion from 23 to 41% over control production (27.9 kg/d) in lactating cows (Bauman et al., 1989). However, increasing increments of bST show less increase. According to the report of Etherton and Bauman (1998), greater increases occur when the management and care of the animals are excellent. This claim might have some validity if it could be shown that high yielding cows prior to bST injection show consistently greater yield responses. In low yielding cattle, dramatic effects on bST have been reported, e.g. a 288% increase in yield in *Bos indicus* cows (Phipps et al., 1991) treated on days 75-95 of lactation, although between days 96 and 120 there was no significant effect on yield.

In addition to the above report the production response increases with increasing dose of bST up to a maximum response at 30-40 mg/day (Bauman, 1992). The commercial preparation in use in the USA is a slow release formulation in which 500 mg are administered every 2 weeks. Although responses to bST are often described as 'smooth' (Bauman, 1992), periodic injections produce an unphysiological lactation curve. Thus, the results of Eppard et al (1991) show that the milk yield curve has a distinctly 'saw-tooth' appearance: during the 2 week period between injections the yield increased approximately 50% in the first 7 days, declining to baseline by day 14, before being sharply stimulated again by the next injection. In the case of 28 day injection cycles a lower than expected milk yield can be obtained in the fourth week (Vernon et al, 1988).

Daily administration of exogenous bST derived from the extracts of pituitary glands, or even the growth hormone release factor from the extracts of the hypothalamus (Enright et al., 1988) of slaughtered cows or recombinant derived bST, cause a higher milk-yield without altering the gross composition. In a long-term study with Holstein cows, bST treatment increased the average fat-corrected milk (FCM) yield in a dose dependent fashion from 23 to 41% over control production (27.9 kg/d) in lactating cows (Bauman et al., 1989). However, increasing increments of bST show less increase. In another experiment, 32% increase of milk-yield was reported in cows treated with 100 IU/day of bST over control (Eppard et al., 1985a); they also found a pattern of diminishing marginal response of milk-yield to increasing hormone dose. Similar results have been reported by other workers (Eisenbeisz et al., 1990; Elvinge et al., 1988; Soderholm et al., 1988). Administration of bST, either by daily injections or in a sustained release vehicle, had no significant differences in milk or solid corrected milk of treated cows (McGuffey et al., 1990). In a previous study it was shown that bST administered by prolonged release formation was effective in improving milk-yield and productive efficiency of cows (Bauman et al., 1989).

Increase in milk production of cows given bST at their peak lactation was less than for those treated at mid to two third of their lactation (McDowell et al., 1987; Richard et al., 1985). The cows receiving 41.2 mg/d of bST in their early lactation reduced 10% more 3.5% than the control group (Schneider et al., 1990). This increase was less than that reported by other workers in the cows treated with bST after their peak lactation (Elvinger et al., 1988; West et al., 1990). This indicated that, even though responses: to exogenous bST did occur, the response was much less than that after peak lactation. One explanation of this was that during early lactation the response might be limited by nutrient availability, because cows were in considerable negative energy balance. The other reason was limited supply of glucose for lactose rather than by the ability of cows to mobilize body-reserves in support of lactation (Richard et al., 1985).

Milk Composition

The complex composition and unique biophysical properties of milk can easily be disturbed by slight deviations in composition. Nevertheless, the cow receiving bST seems to have the ability to produce more milk with the same mammary gland, while retaining normal product composition (Sarwar and Tanveer, 2002). This has probably much to do with the physical limitations for the composition of milk, as mentioned by Walstra and Jenness (1984) which was cited from (Sarwar and Tanveer, 2002).

Bovine somatotropin does not change the composition of milk in any significant way. The concentration of fat and protein in milk varies due to genetics, stage of lactation, age, diet composition, nutritional status, environment and season (Enright et al., 1988). These factors also affect the composition of milk from BST-supplemented cows. Any minor differences in milk composition from bST supplementation are within the normal range. The variations in the content of fat and protein in milk are of the same magnitude as those usually observed in cows not supplemented with bST (Eppard et al., 1985). Lactose percentage decreased significantly at peak lactation but no change was noted at mid lactation in the milk of bST treated cows (McDowell et al., 1987) however, protein concentration declined in cows with negative energy balance (Asimov et al., 1988). This was in line with that of the

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report of Eppard et al. (1985) and Escher et al. (1988) that bST supplementation does not alter the proportion of total milk protein represented by whey proteins and caseins.

Milk from cows supplemented with bST does not differ in the quantity of vitamin A, thiamin, riboflavin, pyridoxine, vitamin B-12, pantothenic acid or choline; the content of biotin increases slightly (Eppard et al., 1985; Escher et al., 1987). BST naturally occurs in cows' milk in very small quantities (only 0.000006 % of all the milk protein is bST). Supplemental administration of bST does not affect the quantity of bST found in milk. Another protein hormone found in milk, insulin-like growth factor I (IGF-I), is regulated by bST. Because the biological effects of IGF-I are not species-specific, as they are for bST, some opponents suggested that this poses a safety concern. When bST is administered to dairy cows, the concentration of IGF-I in blood increases about three-fold and the levels of IGF-I in milk can increase up to two-fold (Asimov et al., 1988; Eppard et al., 1985a; Firkins et al., 1989). Nonetheless, IGF-I in milk does not pose a safety risk because it is a protein and is digested like all other dietary proteins (Farries, 1989). Furthermore, IGF-I is present in human breast milk, and at levels as high or higher than the levels in milk from bST-supplemented cows (Gertler et al., 1984)

Nutritional needs of dairy cows

Studies have examined the production responses to bST under a wide variety of feeding programs. Obtaining a response in milk production to bST does not require special diets or unique feed ingredients. It is important that the diet meet the cows' nutrient requirements which are influenced by the milk yield. Cows supplemented with bST increase their feed intake to provide the extra nutrients needed to sustain the increased milk production, but the nutrient composition and density of the diet do not need to be modified. Cows typically adjust their voluntary feed intake upward within a few weeks after initiation of bST supplementation (Davis et al., 1988; Desnouveaux et al., 1988). Thus, to maximize the milk response to bST, dairy farmers must be attentive to management factors that affect food intake. High quality forage is a critical component in obtaining high levels of voluntary intake.

Other important factors that farmers must consider to optimize the response to bST are: adlibitum feeding (free access to feed at all times), unlimited access to clean cool water, nutritionally balanced diet, adequate dietary protein, proper levels of digestible fiber and control of temperature and humidity. If cows consume an insufficient quantity or imbalanced composition of nutrients, the response to bST will decrease according to the extent of the inadequacy (Asimove et al., 1988)

Body condition

The mechanism of action of bST involves a whole range of changes in the metabolism of body tissue so that more nutrients can be used for milk production. These changes involve direct effects on tissue metabolism (e.g., adipose liver). The difference between body condition of treated and control animals varied between 0.2 and 0.5 points (Wells 1995, Chilliard 1988, Phipps 1990). On the other hand, BST treated cows might have an increased voluntary feed intake starting 4 - 6 weeks after the onset of the treatment (FOI 1993, Oldenbroek 1990). The body weight of a BST treated animal has been recorded as approximately 40 kg higher than control animals at the end of the lactation. However, body composition changed and this effect may be largely due to an increase in body water (Oldenbroek, 1990; Wells, 1995; Chilliard, 1991).

Animal health effect

Several studies have focused on the potential adverse effect of the long-term exogenous administration of bST on health aspects of dairy cattle. Not all studies were very informative concerning study design, diagnoses etc. Conclusions such as "no health effects were noted" have been stated regularly (Phipps 1990, Hartnell, 1991, Burton 1994; Oldenbroek 1990). In general health effects are difficult to detect, because symptoms are often non-specific and therefore, the prevalence and incidence of different health diagnoses, based only on visual or physical examinations are of limited value. During BST treatment an increased number of cows experienced periods "off feed" (reduced feed intake) (Monsanto, 1996; Kronfeld, 1994; Cole, 1992; Pell, 1992). There is no indication in the literature that bST treated animals might have an increased incidence of ketosis (Burton, 1994). Several studies showed an increased incidence of bloat, indigestion and diarrhea in bST treated cows (FOT NADA 14-872 1993; Monsanto 1996) In addition, the incidence of left displaced abomasum tended to increase bST treated animals (Monsanto 1996). In general the control animals had more miscellaneous health problems during the pre-treatment period than the bST treated animals. This difference might have influenced the outcome of the study (Monsanto 1996). Several authors have described increases in laboured breathing, body temperature and heart rates in BST treated animals (Cole 1992; Monsanto 1996). One manufacturer of bST warns that udder oedema is more likely in bST treated cows, especially when bST use is commenced in mid-lactation.

Heat stress

The increased metabolic activity associated with bST induced galactopoietics also involves an increase in heat production by the body, which challenges thermoregulatory processes. The effect can be pronounced, as illustrated by the report that, of 18 cows receiving bST and subjected to heat stress, two cows died and four suffered from ataxia, whereas no such responses were observed in 16 control cows (Elvinger et al., 1992).

Life span (culling)

Concern has been expressed that cows might be metabolically overworked when treated during their lactation with bST. Therefore, life-expectation of the bST treated cows might be reduced. This effect of bST might be visible in an increased percentage of involuntary culling in herds However, the decision to cull dairy cows is complex and affected by many cow and farm factors (Pikus et al., 1989). Only limited information is available on culling rates associated with bST treatment. This is because of the above described reason and the fact that culling was prohibited in several of the studies. PAMP data (1996) showed that more cows had been removed from the bST treated herds than from the control herds. The difference was significant in multifarious cows. Ruegg et al. (1998) focused in their study on the culling practices of 32 herds. In 19 herds cows were BST treated. During the course of the study, 4 farms discontinued or restricted the use of bST and two control herds commenced bST treatment. These farms were excluded from the study. Culling rate was higher in the bST treated herds than in the control herds, although the difference was not significant. In the bST treated herds, more cows were culled because of mastitis and sickness and fewer cows were culled for reason of production or death, than in the control herds. A problem with this study was that the control and bST treated herds appeared to have considerable differences in herd size, milk production levels and age at first calving. Cole et al. (1992) presented a study on health and reproduction of bST treated dairy cows. No culling was conducted during the study and cows were only removed for scheduled necropsies or unscheduled necropsies when a cow died or was declared moribund. Eight cows had unscheduled deaths, and all these animals were bST treated. The following diagnoses were included, four mastitis cases, two pneumonias, one abomasal displacement and one case of Johnes disease. Other studies did not reveal a high culling incidence of bST treated animals compared with control animals (Oldenbroek, 1990).

Causing disease and medicine usage

BST increases the frequency of certain disease conditions such as mastitis and foot problems in cows. These conditions are normally treated using veterinary medicines. Hence bST is leading, on average to the increased use of veterinary medicines. This increased use allows more opportunity for the development of resistance to antimicrobials in pathogens on farms (Pocius et al., 1986). It may also result in increased residues of antibiotics in milk. These residues could result in further resistance to antimicrobials when the milk is fed to calves or other animals.

Human health

Consumers can be reassured of the safety of milk from cows supplemented with rbST based upon the U.S. experience. Milk from rbST-supplemented cows (more than 265 billion liters [70 billion gallons] from more than 30 million cows as of 2009) has been a part of the U.S. food supply since rbST approval in 1993 and its use has not been associated with any scientifically documented detrimental effects on human health (Raymond et al., 2010). This was associated with the report of (Hammond, 1990; Bennett, 1950; Froesch, 1957) in the 1950s, there was interest in giving bovine growth hormone injections to children who were deficient in human growth hormone to help them achieve normal growth. Unfortunately, in these children, it was shown definitively that bovine growth hormone had no effect on growth in humans. This means that even if milk had high concentrations of bovine growth hormone, the hormone would not stimulate human cells to grow. Furthermore, when bovine growth hormone is given orally, it is broken down by digestive enzymes. According to the Office of Biotechnology at Iowa State University, the "biological activity of commercial bST is identical to natural bST." Bovine somatotropin ingested via a human's digestive system has no effect on the human. The digestive system breaks the bST down into amino acids and peptides, which remain inactive. Human growth hormone (or human somatotropin) has different amino acids than bST, which prevents bST from having any effect on humans. Milk produced by bST injected cattle is perfectly safe for human consumption.

CONCLUSION

Generally utilizing of bST hormone can alleviate the demand of milk due to an increment of human population. bST hormone increases milk production in dairy cows while with normal milk composition or with no altering milk composition. It is a metabolic hormone. Cows supplemented with bST increases feed intake. It also increases the treated cow's body weight. It has no any effect on animal health. In addition to this it has no any effect on human health a person who is consuming a milk gained from BST hormone treated cow. Therefore, according to the recommendation of FAO utilizing of bST is an advantages for increment of milk production and full filing the standard milk intake per individual per year of an individual person like for developing countries.

DECLARATIONS

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Author's contribution

MS Kibrnsh Tegenaw and MR Assemu Tesfa have been involved in critically revised the manuscript for important intellectual contents. MR Shewangzaw Addisu wrote the manuscript. All authors read and approved the final manuscript.

Competing interests

The authors declare that they have no competing interests.

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