

Bovine Somatotropin: An Overview

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Introduction

Bovine somatotropin (bST), or bovine growth hormone, is a natural substance produced by the pituitary gland, a small structure at the base of the brain. Growth hormone is produced in all species of animals and is important for growth, development, and other body functions. In the 1930's, it was discovered that injection of bST into lactating cows resulted in a significant increase in milk production.

Until recently, the only source of bST was from the pituitary gland of slaughtered cattle. Only small, expensive quantities were available. The advent of biotechnology led to the isolation of the gene that "codes" for, or controls the production of bST. Scientists, using a technique known as recombinant DNA technology, removed the gene from the nucleus of bovine pituitary gland cells and inserted it into the bacterium *Escherichia coli*. These genetically altered bacteria are then grown in artificial media and produce large amounts of bST which is then purified and injected into cattle. Similar recombinant DNA technology is used to produce several approved drugs, including insulin for treatment of diabetes and tissue plasminogen activator (TPA) for treatment of coronary thrombosis (heart attack) in man.

In agriculture, biotechnology has often been viewed as either a panacea for curing most problems, including the elimination of world hunger, or damned as a threat to the environment and the economic viability of the family farm¹. The potential licensure of bST for commercial use in dairy cattle has been controversial and has stirred heated debate by the dairy industry, activist groups, politicians, and consumers. Four commercial companies are in the process of submitting data to the Food and Drug Administration (FDA) for approval to use bST in dairy cows to increase milk production.

Effects on Production

Since bST is a complex protein, it is immediately broken down into small, inactive amino acids and peptides when ingested. BST must be given by injection on a regular basis, similar to insulin in people who suffer from diabetes. Commercial bST products will be administered by this route. The frequency of injection will depend on the formulation of sustained release products.

Milk yields are significantly increased when cows are treated with bST, although not as much as some reports in the popular press have indicated. All of the precise mechanisms for increasing milk production are not known, but blood flow is increased to the mammary gland, resulting in an increased availability of nutrients available for milk

production. There is also an increased extraction of non-esterified fatty acids by the mammary gland, which increases 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. There is an increase in absolute feed intake by bST treated cows, however. Milk yield increases from 2.2 to 5.2 kg (4.8 to 11.2 pounds) per day and feed efficiency improves from 2.7 to 9.3%.² Table 1 summarizes trials in several states and foreign countries (32 week treatment):

Table 1. Increases in Milk Production and Feed Efficiency of bST Treated Cows²

Location	Increase in Milk Yield (%)	Increase in Feed Efficiency (%)
Arizona	8.3	2.7
Cornell University	11.5	5.3
Missouri/Monsanto	21.8	8.2
Utah/Utah State U.	14.6	5.3
France	17.8	9.3
Germany	16.6	4.9
Netherlands	18.5	7.6
United Kingdom	19.2	5.4

Galligar and Chalupa summarized several trials and found a production increase of 3.8 kg (8.36 pounds)³. They estimated that, depending on management capabilities, responses in treated cows are expected to range from 8.5 to 17.6%. Grain used to meet the needs for this increased production would increase from 10 to 30% and forage consumption would increase from 0.6 to 10.5%. Milk yield gradually increases for the first few days after treatment begins, and maximum increase is seen in about 6 days.

Normally, cows reach peak production a few weeks after lactation begins. Production then slowly declines throughout the remainder of lactation. The ability of cows to maintain relatively high levels of production throughout lactation is referred to as persistency. The major response of cows treated with bST is a significant improvement in persistency. There is a marked reduction in the normal decline in milk yield as lactation progresses. The response of treated cows in early lactation is fairly small³.

"Misinformation by groups that are antitechnology, against use of food animals, and those with a hidden agenda, tends to give the impression that controversy exists concerning the biology of somatotropin. Eight hundred reports on 20,000 treated cows have yielded remarkably consistent results worldwide"³.

It is difficult to predict the response of individual cows to bST. Quality of management, including health programs, milking practices, nutrition, cow condition, and environmental conditions will be the major factors in the response to bST. Cows show a slightly higher response when treatment is started at day 101 of lactation rather than days 57-100. Multiparous cows show a greater response than first lactation heifers².

Effects on Cow Health

The physiological effects of bST treatment are the same as those seen in any high producing cow. The management changes instituted by producers in anticipation of using bST will probably cause a greater increase in milk production, efficiency, and profitability than actual use of the drug⁴. In the initial stages of use, producers will be encouraged to begin use of bST on cows at least 100 days into lactation, in good physical condition, and free from health problems such as mastitis or infertility. Concern has been expressed regarding the effect of bST on reproduction. The optimum calving interval of 12-13 months may lengthen due to bST altering the shape of the lactation curve.

DHIA records show that higher producing herds have lower conception rates than low producing herds⁵. This negative effect on calving rate is seen in cows treated with bST and is consistent with the increase in production. Effect on reproduction is affected by condition, nutritional status, and health, as well as by dosage of bST. Few studies have investigated the physiological effects of bST on ovarian and pituitary function. Cows on a high dosage of bST show an increase in length of estrous and reduced activity when in heat. This effect is not seen on low to average dosages of the drug. High dosages of bST (50 mg/day) are reported to increase embryonic death, and initiation of treatment during early pregnancy should probably be avoided⁵.

Eight studies show no association with increased mammary infections⁵. Overall, 13% of control cows and 15% of bST treated cows had mastitis. Gestation length, calf birth weight, calf viability, and calf growth have not been influenced by using the drug. Some early reports indicated an increased incidence of twins, but later trials contradicted this.

Many health problems of dairy cows are associated with calving and rebreeding, so that an increased calving interval in treated cows could benefit the health status of treated cows.

Milk Composition and Safety

Consumer advocates and others have expressed concern regarding the safety of milk from bST treated cows. The characteristics of milk from bST treated cows is within the normal range of variation of milk from untreated cows.

All milk contains natural bST that is produced by the cow. Milk from treated cows also contains small amounts of bST. Since the hormone is a protein, it is immediately broken down into inactive amino acids and peptides in the digestive tract when consumed. Steroid hormones such as estrogens, progesterone, and anabolic steroids taken illegally by athletes are smaller, ring-like structures that are absorbed from the digestive tract and are biologically active in man.

This is not the case with bST, whether produced naturally by the cow or by recombinant DNA technology⁵.

Bovine somatotropin is inactive in man, even when injected. During the 1950's, natural bovine somatotropin was injected into children with growth defects and found to be biologically inactive. The bovine somatotropin protein molecule differs from human somatotropin by about 30% of the amino acid sequences. There are four forms of natural bST and each has either 190 or 191 amino acids. Recombinant bST injected into cows has 191 amino acids. One company's product differs by only one amino acid on the end of this chain. The biological inactivity of bST in man and the fact that it is completely degraded in the digestive process means that the small amount of recombinant bST in milk from treated cows is inactive in man.

Milk composition from bST treated cows has been thoroughly investigated⁶. During the first 28 days of treatment, milk fat increases and milk protein decreases slightly. After longer treatment, cows adjust intake and the normal balance is re-established. An increase in non-protein nitrogen and whey protein and a decrease in casein has been observed after long-term bST administration. This difference is not always statistically significant, and the effect on cheese yield would probably be minor, if any. One study showed a slight increase in unsaturated vs. saturated fat. The difference was small but tended toward a more healthful product. No differences in free fatty acids have been observed. No differences in flavor tests have been found. There is possibly a slight increase in cholesterol but it is within the range for normal milk. Insulin-like growth factor I increases by up to two-fold in milk from treated cows but is still well within the range for both bovine and human milk.

Economics

The ultimate economic effect of bST approval and use on the family dairy farm has generated heated debate. The Animal Health Institute, a consortium of drug and vaccine manufacturers, maintains that use of the product will be of equal value to any size farm¹. They contend that use of the product will favor the good dairy manager, regardless of farm size.

Estimates of the effect of bST on dairy production have probably been exaggerated. The USDA estimates that the use of bST could lead to a 2 to 5% increase in national milk production within five years, or about the increase seen every year without the use of bST.

In most dairy herds, the product will not be used in cows prior to about 100 days of lactation. It will not be used in cows with chronic low level disease, fertility problems, and usage may be somewhat less in heifers than adult cows. If 50% of farmers adopt the technology and it is used in 60% of lactation days per user herd, milk production will increase by about 3 1/2%, assuming an average per cow production increase of 15%. Most well managed herds increase per cow production more than this with improved management and genetics on an annual basis. A thorough herd analysis by a competent nutritionist and veterinarian and timely implementation of resulting recommendations will result in a larger increase than use of bST in most herds⁴.

Failure to adopt proven technology is a problem

throughout the dairy industry. Almost 50% of cow breedings in Iowa are to natural service, rather than artificial insemination from proven sires with superior genetic performance. Only 45% of Iowa dairy producers use DHIA management information and records to improve production⁷.

The government milk price support system makes prediction of the effect of bST on milk prices difficult to predict. It is true, however, that efficient managers in areas of the country with higher milk prices benefit more from application of technology and increased production. The present price support system would tend to work to the disadvantage of producers in the upper Midwest, although the degree of this effect is unknown.

It can be argued that the large commercial dairy operation can institute use of bST more easily, rapidly, and efficiently than smaller operations. Sophisticated record keeping and division of labor may make timely injection of cows more feasible. Demands on the labor and management skills of diversified farming operations typical of Midwest dairy producers may make newer technology more difficult to implement.

Others argue that smaller producers with direct owner control of the herd can actually manage individual cows better and will see a greater production increase from use of bST. It is not automatically true that larger herds are better managed and will therefore benefit more from use of bST.

There is no question, however, that if the consumer loses confidence in the quality of milk, whether the reasons are logical or not, consumption and prices will fall. This is a major concern of many dairy producers. The best that can be said about bST is that it is neutral concerning milk quality.

FDA Approval

The Food and Drug Administration has not licensed bST for use in dairy herds. They have, however, approved the consumption of milk and meat from treated animals. Such approval is often granted during the process of license approval of animal drugs. Milk from treated cows has been deemed safe because bST is biologically inactive in man and is a protein hormone which is digested and enzymatically destroyed when consumed. Each sponsor (company seeking approval for bST) has to demonstrate zero activity in milk when ingested. No withholding period following treatment of cows with bST is required. Some fat changes occur during the first few weeks of treatment but this returns to normal. This change is within the normal variation of milkfat. Nutritional and processing qualities are not significantly altered.

"The FDA has found no pertinent information indicating that food derived from bST treated cows is unsafe⁸."

Effectiveness must be demonstrated in expected use conditions before a product can be approved. This must be done in a minimum of 3 geographic locations. Fifty cows per herd were required for bST approval.

Three dosages of the drug were used for titration studies. Use of the drug was initiated at various times during the lactation period. The efficacy and safety for the first and later lactations is monitored. Milk yield was calculated on a 3.5% fat corrected basis. Composition variables including

fat, crude protein, lactose, calcium, and phosphorus are measured about once per week. Daily feed intake was measured in several of the test herds. Body condition and health were monitored throughout the studies. The effect of bST treatment on reproduction, including estrous cycles, conception rates, number of breedings per conception, length of time from parturition to conception, abortions, incidence of twinning, calving difficulties, stillbirths; weight, growth, and health of calves during the first four weeks of life were all monitored. Monthly somatic cell counts, as a measure of mastitis, was required. Injection sites were monitored for any signs of adverse reactions.

To monitor safety, 1, 3, and 5 times expected use level was required for two consecutive lactations in one herd from each investigator. Heifers born to treated cows were raised through breeding age and monitored for abnormalities. Investigators were also required to prove that use of bST was not harmful to the environment.

The quality control of bST used in the trials was monitored and all protocols for investigation were approved before the trials were run. The majority of the trials used in the approval process were done by independent scientists at university laboratories and farms or using commercial herds. FDA rulings on the approval process are expected within a year, pending completion and review of all trials.

Federal law prohibits the social and economic need for a drug to enter into FDA's approval decision. It is the policy of the federal government that producers can decide whether a product is economical or useful, as long as the product is safe, pure, potent, and effective. Approval does not mean that a product must be used, but only that it can be if desired.

Controversies Concerning use of bST

The most intense controversy surrounding possible approval of bST for use in dairy cows has occurred in Wisconsin, Minnesota, and Vermont. In Minnesota and Wisconsin, a one year moratorium on the use of bST was passed by the respective state legislatures. This moratorium expires in the summer of 1991.

Some producers fear that advancing technology will outpace them and they will suffer economically as a result. Others feel that a product such as bST will work to the disadvantage of producers in the Great Lake States and the Northeast. Natural resistance to advancing technology and a fear of the new biotechnology causes some to resist the approval and use of bST. Activist groups with a variety of agendas and motives have addressed the issue. Some have stated that milk from treated cows may not be safe after all and more testing is needed, others see this as a scare tactic to delay or block the approval process and undermine consumer confidence in milk if the product is approved. Some animal rights groups see the use of animals for food, under any circumstances, as inhumane or a violation of those animal's "rights". Others have stated that cows have a right not to be injected with bST.

Other opposing arguments state that the FDA does no independent testing of its own but only monitors the investigators studies. The persistent oversupply of milk and dairy products has also been listed as a reason not to approve use of bST. Some dairy farmers opposed the use of bST but feel

they would have no choice but to use the product in their own herd in order to remain competitive if it came into general use⁹.

Stanton and Novalovic have listed arguments for and against approval of bST in the categories of food safety and the effect on the number and size of farms¹⁰:

Food Safety

Arguments for approval of bST:

1. Safety is not an issue. BST is naturally present in milk, and any recombinant bST present would be broken down in the digestive process.
2. The FDA approval process can be trusted.
3. Consumers will be reassured when they get the complete story of safety of milk from treated cows.
4. Improved efficiency of production will reduce prices.
5. Milk consumption will increase when prices decline.
6. Decreased prices will be an advantage for low income families.
7. Some consumers will prefer "organic" (non-bST treated) milk. Marketers could sell such an "organic" product.

Arguments against approval:

1. Can we really be sure that milk from bST treated cows is safe? Do we really know all we need to know?
2. The FDA is understaffed and over-worked. Their credibility is not high.
3. We won't see lower milk prices. Farm prices from 1981-1998 fell 11%, but retail food prices increased 11% over the same period.
4. Dairy product consumption at best will be unaffected, and more likely will be hurt by approval of bST.
5. Scientists don't really know what sells dairy products.
6. Organizations will work hard to convince consumers that bST is bad.
7. Moratoria imposed by some states will make consumers more wary.
8. Consumers won't believe the chemical companies and FDA when they refute negative campaigns.
9. The dairy industry can't afford to stake everything on what some people say is scientific truth.

Effects on number and size of farms

Arguments for approval:

1. bST is size neutral.
2. Careful management may give an advantage to small farms.
3. Those who implement bST effectively soon after approval will have an advantage.
4. Saying that small farms can't handle this technology is wrong.
5. Farm size has been increasing and number of dairy farms has been decreasing for years. This will occur with or without approval of bST.
6. bST will give smaller farms a chance to improve performance.
7. Manure and waste management will slow the switch

to large farms.

8. bST will assist farmers who are low cost producers, regardless of farm or herd size.

Arguments against approval:

1. Economies of scale work against the small producer.
2. Feed and forage is more difficult to produce on smaller farms.
3. Small farms will be pushed out faster. Farm buildings and other assets will be worth less as more producers are forced out of dairy production.
4. There will be a period of over-supply of milk.
5. In the Northeast and Midwest, fewer farms will result in decreased service and supplier support for remaining farms.
6. bST is one more thing to buy, one more risk to take.
7. Uncertainty increases risk. This works to the disadvantage of small farms.
8. The financial spread between small and large farms will get wider.
9. There is an adverse effect on the environment and quality of life when large farms are favored.

Summary

Approval and use of bST is highly controversial and will have a significant effect on research and development investment in biotechnology in agriculture by commercial firms. Universities will face the difficulty of presenting scientific information in a manner that both is and gives the appearance of being unbiased. An era of a direct challenge to technology itself is relatively new to most professional agriculturalists. Patience, tolerance, and understanding will be required by educators, extension workers, and other professionals in agriculture who work with groups that both support and oppose implementation of technology such as bST.

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