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Enhancing Dairy Yield: Innovations on Artificial Induction of Lactation in Cows

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ABSTRACT

This review was undertaken to examine the function of artificial induction of lactation and in economic importance of artificial induction of lactation in dairy cows. The narration-style presentation of the relevant scientific references is sourced from many websites. Stimulation of the udder and teats (e.g., by massage) at the time of milking causes the release of prolactin. Lactation-induced cows produced 65% of the milk yields achieved by 150 days in milk (DIM) as compared to non-treated cows. Synchronizing estrous cycles with prostaglandin PGF2α injections improves success rates of induced lactations, but not milk yields. Recombinant somatotropin induction in tropical regions shows limited studies, affecting response to treatment, compared to temperate climates. Milk production is increased by using growth hormone, Bovine somatotropin (bSTr), and reserpine injections. Releasing prolactin on days 13-16 and 8-10 increases success rate from 40% to 100% in cows (success > 9 kg milk/d at peak yield). Artificially inducing lactation in nonpregnant cows leads to lower days to first service as compared to non-treated cows using estrous and ovulation control regimens. In conclusion, this review confirms that reproductive performance and milk composition are not adversely affected by the artificial induction of lactation. Prolactin supplementation can increase the amount of milk produced in artificially induced lactation cows by providing more proof that the hormones (estrogen, progesterone, prolactin, and glucocorticoids) interact synergistically to initiate lactogenesis. Significant culling of high-producing cows with low fertility reduces the profitability of dairy farms as those cows are replaced with heifers. Therefore, artificially inducing lactation in nonpregnant cows may be a management alternative to reduce culling and increase profits. This approach gives owners a fantastic choice for keeping a herd with high genetic potential for milk production, avoiding unproductive animals in the herd, fostering new prospects for reproduction, and boosting earnings.

Keywords: Artificial Induced Lactation-mechanisms, Dairy Cow, Economics, Prolactin and Somatotropin

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INTRODUCTION

The dairy business is expected to expand by 26% globally over the next 10 years in both distribution and growth [1]. The steady growth in South Africa, as reported by Melissa *et al.* [2], was 4.8% in 2018 and 3.0% in 2017, exceeding the 2.2% increase in worldwide milk production in 2015. But in 2016 there was a 0.1% modest decline [3]. According to Melissa *et al.* [2], there will be a 1077-million-ton production of milk by 2050. By 2025, Ethiopia's population is expected to reach more than 140 million, placing additional strain on the country's already-struggling food production sector, which includes the dairy sector [3]. Ethiopians consume less than 20 liters of milk per person per year as compared to the global average, leading to a large gap between demand and supply. Production of high-quality milk is a challenge due to growing population growth and issues with milk supply [2].

In dairy herds, involuntary culling of cows can lower milk production per hectare per year and is frequently caused by reproductive failure. Reproductive failures were the root cause of 27.7% of culling rates in a retrospective study done in Brazil from 2000 to 2003. Because reproductive features are unpredictable, producers frequently use artificial induction of lactation as a way to prevent unintentional culling [4]. Dairy cow induction protocols have been devised for use in practical farm settings, enabling producers to reduce herd culling losses and replacement costs [5,6]. Long calving intervals and considerable non-voluntary culling losses might result from reproductive problems and failure to breed. Producers can preserve genetically superior milk production potential and benefit from more breeding opportunities by artificially inducing lactation in cull cows; however, this practice lowers milk sales profit and increases reproduction costs [7]. Using estrogen and progesterone during the past 60 years, a variety of strategies have been used to grow the mammary gland and start lactation. A 120–180-day injection schedule is part of these treatments. However, the success rates and milk production were often poor with these long-term treatments.

Dairy farms are less profitable as a result of the significant culling of high-producing cows with low fertility since heifers are used in their place. A management strategy to boost earnings might be to force lactation in non-pregnant cows. One of the most expensive aspects of dairy production is the addition of replacement heifers to the milking string. A single heifer must be reared for 25 to 26 months at a cost of $1150 to $1350 [8]. Reducing the requirement for replacement heifers by increasing lactation in non-pregnant cows and selling extra heifers could boost income. Smith and Schanbacher [9] demonstrated that a 7-day estradiol-17 and progesterone therapy period might induce lactation. The goal of their treatment was to emulate the high levels of these hormones seen in the final month of pregnancy in cattle, when the mammary glands expand significantly. However, induced cows given with reserpine to boost prolactin concentrations produced more milk than controls [10,11] demonstrating a role for prolactin in induced lactation. According to Byatt et al. [12], on treatment days 8 to 14, induced heifers treated with recombinant bovine prolactin (rbPRL) did not differ from their induced controls in terms of total mammary DNA. However, the rbPRL therapy promoted mammary differentiation and increased the weight of dry tissue.

According to several investigations, milk production in induced animals is 60–70% of previous lactation yield [6,10,13,14]. According to the hypothesis put forth by Fowler et al. [16], inadequate differentiation of secretory cells rather than insufficient mammary tissue proliferation caused lower than normal milk production in induced animals. There was still a lot of variation in milk yields between lactation-induced cows, despite the fact that the new technique was effective in 60% of treated animals. Numerous modifications have been used to increase success rates and decrease variability in milk yields since the inception of this shortened process [10,15,17]. Somatotropin injections have been used to increase milk yields, with 28.3 kg/d compared to 24.1 kg/d in controls.

Smith and Schanbacher [9] demonstrated that lactation can be induced by administering 17-estradiol (1 mg/kg BW) and progesterone (0.25mg/kg BW) to cows for seven days. Erb et al. [18] observed that cows with more effective induced lactations had lower plasma levels of estrogen and progesterone than before. The goal was to produce high steroid concentrations in the final month of pregnancy with high rate of mammary development. Investigations extended treatment time but failed to improve lactation induction or eliminate variation in milk output. Collier et al. [10] used reserpine injections with estrogen and progesterone to induce prolactin release and improve lactation induction. According to Magliaro et al. [19], progesterone and estrogen-induced dairy cows produced more milk when given bSTr. Animals given bSTr generated 21.9% more milk than cows not given the hormone. A 21-day strategy with increased dosages of estradiol and progesterone, prostaglandin analogs, and bSTr was suggested by Mellado et al.

In order to be employed as a management tool on dairy farms, artificial lactation must be economically viable. Allaire *et al.* [20] and a more recent report [21], 26.7% and 47%, respectively, of cows between the ages of 3 and 8 years are eliminated because of reproductive problems. For artificial lactation to be employed as a management tool on dairy farms, it must be financially feasible. The current review focuses on the use of artificial lactation induction in dairy cows and its economic significance. It also looks at how dairy cows are artificially induced to produce milk. In just a few papers has the economic value of using induced lactation technology been quantified using a dairy systems approach.

Objective

- Reviewing the purpose of artificially triggering lactation in dairy cows
- To review the economic value of artificially triggering lactation in dairy cows

LITERATURE REVIEW

Definition of Terms

Bovine somatotropin (bST), also known as bovine growth hormone, is an animal drug approved by FDA to increase milk production in dairy cows. This drug is based on the somatotropin naturally produced in cattle [22]. rBST is carried to the liver where it stimulates that organ to produce Insulin-like Growth Factor (IGF-1), a protein hormone that aids in turning nutrients to milk. IGF-1 is carried to a cow's mammary gland where it stimulates milk production. Studies have found that rBST can increase milk production 10% to 20% [14].

Protocols for Artificial Induction of Lactation and Other Factors in Dairy Cattle

Induced lactation may be an alternative for cows with low fertility but high yields. Artificial induction of lactation by the use of hormones can be used as a substitute to natural lactation, minimizing culling losses in the herd and increasing revenues. It should only be used when the animal has been rendered infertile and all other treatments for reproductive diseases or anomalies have failed [14]. Breeding is more successful because lactation brings animals into lactation, causes estrus, and some of them get pregnant. After a week, this method's milk is typically acceptable for ingestion by humans and has a composition similar to milk produced after a regular calving.

Numerous reproductive issues, such as repeat breeding, anoestrus, chronic cervicitis, pyometra, or congenital abnormalities like free martinism, underdeveloped ovaries or genitalia, anatomical flaws (such as persistent Mullerian ducts), and hormonal dysfunction (such as cystic ovaries), result in the culling of hundreds of thousands of high-producing dairy cows and buffaloes each year. Due to reproductive issues, between 27 to 47% of dairy cows are destroyed [24]. It is an issue that exists everywhere. Farmers may experience less financial loss as a result of the infertility or sterility of their high-yielding dairy cows and buffaloes when lactation is artificially induced by hormone therapy or other medications. According to research by Magliaro et al. [19], hormonally treating nonbreeding cows to induce lactation is more profitable than buying replacement heifers. With the help of this technology, the herd can regain its production capacity while also addressing its nonresponsive reproductive issues.

Lactation and peak yield: According to Yanga and Jaja [24] assert that the procedure includes both milk secretion and removal from the mammary gland. It consists of two stages: lactogenesis, which uses the hormones prolactin and glucocorticoids, and gatactopoiesis, which is the continuation of lactation using growth hormone. Additional variables that could influence milk composition include breed, genetic variety, health, environment, management practices, and nutrition [25].

Induced animals have similar or greater daily and peak milk yields to cattle in tropical countries [9]. The daily mean (11 kg) and peak (15 kg) yields for the induced animals was favorable compared with the daily average of 10 kg for untreated cattle while the time to attain peak milk production for un-stimulated cows was 8.7 ± 1.8 weeks and 12.7 ± 1.8 weeks for the stimulated animal [26]. Induced cows may have delayed peak yield due to less secretary tissue at the beginning of lactation, as compared to non-induced cows [27]. Induced cows are also less sensitive to cell proliferation and have a longer postpartum period of secretory tissue proliferation. Uncoupling and slower recoupling of the somatotropic axis can also delay mammary development and prolong maximum parenchyma volume [29].

Prerequisites for artificial induction: It is an easy and affordable procedure with quick protocols that achieve high success rates with more milk produced for longer periods of time. As there have been no reported adverse effects on human health, it is safe for intake by humans [29].

Selection criteria and importance of hormone: For milk production, the animal should be healthy and in good physical condition. It is desirable to use repeat breeders or anestrus cows with clinically healthy udders and teats. Animals that are dry and not pregnant can also use it [24]. In bovines that are well-fed and have an ideal level of protein in their diets, the treatment is more successful. The development and operation of the mammary gland are significantly influenced by hormones. For the purpose of inducing lactation, several medication combinations are employed. The combination of estrogen and progesterone stimulates the growth of the mammary glands lobule-alveoli [19].

Induction protocol used: Protocols used for induction of lactation in cows and buffaloes: Infertile, non-lactating, non-breeding cows and buffaloes have been made to induce lactation using a variety of different techniques [19]. The following are a few of these protocols that have been scientifically verified and practically tested by veterinary professionals.

Table 1. Treatment Schedule for Induction of lactation

Treatment	Dose	Day of Study	Delivery Route
17B-estradiol[a]	0.1mg/kg body weight	0-6	Subcutaneous
Progesterone[a]	0.25mg/kg body weight/day	0-6	Subcutaneous
Bovine sosmatotopin (posilac®)[b]	500mg	0,10,20,30, and about every 14 days thereafter	Subcutaneous
Dexamethasone [c]	0.05mg/kg body weight	13, administered 24 hours prior to first milking	Intramuscular

Protocol # 1: Smith and Schanbacher [9,13] and Smith et al. [9] daily doses of 0.1 and 0.25 mg/kg each of estrogen and progesterone1 body weight per day for a week. Some cows didn't react. Milk production was comparatively high in cows in which lactation was successfully induced (60 percent of treated cows). Exhibiting aberrant estrous behavior for up to 20 to 50 days after ceasing the estrogen injection was a significant undesired side effect of high estrogen dosages.

Protocol # 2: Twenty dry Holstein cows with reproductive issues who had failed to become pregnant were used to test the Freitas et al. (2010) technique Protocol:1. Day 1, 8 and 21: Recombinant bovine somatotropin (bSTr, 500 mg), 2. Day 2 to 15: Estradiol benzoate (0.071 mg kg 1 per day subcutaneously), 3. Day 2 to 8: Medroxy progesterone acetate (0.25 mg kg 1 per day, subcutaneously), 4. Day 19: Prostaglandin F2á (0.530mg, subcutaneously), 5. Day 19-21: Isoflupredone acetate (0.05 mg kg 1) Intramuscularly, 6. Massage of teats and udder for 5 minutes daily from Day 17 to 21. Milking carried out from 22nd day of induction. , 7. bSTr was injected every two weeks after induction of lactation. And 8. Mean milk yield with this protocol was 21.9±2.9 kg day.

Season: Photoperiod is one of the most important environmental factors affecting milk yield [30]. As for lactogenesis, increased secretion of prolactin is an important factor which is further associated with increased temperatures and longer photoperiod [31]. Complete treatments during warmer months, the success of the induction scheme in prepubertal heifers is increased [6].

Reproduction: Smith and Schanbacher, [9] have reported that following induced lactation animals exhibit intense estrus activity. Hormonal induction has no apparent effect on reproduction; natural lactating and induced heifers averaged 1. 2 inseminations each. Time taken to exhibit estrus after hormonal treatment (87-231 days) was longer in buffaloes as compared to cattle (91-152 days). 30-90%

pregnancy rates are reported after artificial induction of lactation [32]. 41.4% cows having reproductive problems have been reported pregnant after artificial induction of lactation [33]. The difference in conception rate may be due to variation in feeding regimes, detection of estrus and time of insemination.

Functions of hormones and drugs during artificial induction

Estrogen and progesterone: Estrogen stimulates development and growth of mammary gland ducts. Estrogen and progesterone in combination stimulate development of lobule-alveolar tissue (milk producing tissue) of the mammary gland. Estrogen additionally helps in initiation of lactation in two ways. Firstly, it causes release of prolactin from the anterior pituitary gland into the blood. Secondly, it causes an increase in prolactin receptors in mammary cells [34].

Glucocorticoids (e.g. cortisol and dexamethasone): Glucocorticoids cause alveolar cell differentiation of the mammary gland. They compete with the progesterone for binding sites on the mammary epithelial cells. Injecting glucocorticoids to dry cows which have already been treated with estrogen and progesterone (and thus have a developed mammary gland) helps in the induction of lactation. An increased level of glucocorticoid as a result of dexamethasone injection would displace progesterone from the receptors on mammary cells, thus reducing the inhibitory action of progesterone on the synthesis of prolactin receptors [35].

Prolactin: Prolactin is released from anterior pituitary gland. Its main function is lactogenesis and not galactopoiesis. Stimulation of udder and teats (e.g. by massage) at the time of milking causes release of prolactin [36]. Prolactin is not required for milk production after lactation has been established.

Bovine somatotropin (bSTr, growth hormone): STr is used to increase milk production. Magliaro et al. [19] evaluated the efficiency of bSTr in the increase in milk production in dairy cows artificially induced into lactation with estrogen and progesterone and observed that bSTr treated cows produced 21.9% more milk when compared to induced cows that did not receive bSTr. Growth hormone increases milk production by partitioning of available nutrients away from body tissues and towards milk synthesis.

Role of prostaglandins (e.g. PGF2á): For artificial induction of lactation PGF2á is used to induce luteolysis which brings all treated cows and buffaloes in a uniform phase of the estrous cycle. This uniformity may eliminate variations among animals related to differences in concentrations of estrogen, progesterone, glucocorticoids and prolactin at the time of initiation of lactation. In addition, removing the progesterone source (corpus luteum) by PGF2á may allow induced cows to be more responsive to reserpine and dexamethasone treatment following the initial estrogen and progesterone treatment [37]. It also allows glucocorticoids to displace progesterone from binding sites in mammary tissue, thereby removing the progesterone block to lactogenesis. Thus, use of PGF2á to induce luteolysis offers the opportunity to initiate a lactation induction protocol during very different stages of the estrous cycle; estrus and metestrus when progesterone is low and estrogen is elevated or diestrus when progesterone is the dominant steroid hormone [37].

Thyroid and parathyroid hormones: Thyroid hormone is an iodine containing hormone that increases the basic metabolic rate of the animal. Owing to loss of iodine in the milk, during lactation, the mammary gland is in a euthyroid state while the rest of the body is hypothyroid [38]. During lactation, parathyroid hormone is responsible for removal of calcium from the bones and adding it to the blood for milk synthesis.

Insulin: In cattle, insulin is involved in mechanisms partitioning nutrients away from synthesis of milk and towards body tissues. Thus, higher the insulin consideration, the lower the milk yields [39].

Reserpine: Reserpine (an alkaloid obtained from the roots of Rauwolfia serpentina) is used to stimulate release of prolactin and its use decreases the variation in milk production amongst animals as well as it shows an increase in the induction of lactation rate [40].

Artificial Induction of Lactation of Cows

Estrogen, progesterone, prolactin and glucocorticoids work *synergistically* at the onset of lactogenesis. Estrogen stimulates mammary ductal growth, and the combination of estrogen and progesterone regulates lobular-alveolar development of the mammary gland [41]. This development does not occur in infertile animal or animals suffering from reproductive disorders due to relative absence of sex steroid hormones.

Artificial induction of lactation can be induced in such animals by the combination of steroid hormones estrogen and progesterone. Additionally, reserpine (tranquilizer-increases prolactin level) and Dexamethasone (a synthetic glucocorticoid) can be used in induction protocols to increase the success rate [42]. Artificial induction reduces the involuntary culling rate as well as the genetic losses. To save such genetically superior bovines, induction of lactation is the most appropriate technology used under tropical conditions. The treatment is more effective in well-fed animals with good body condition score and having normal teat and udder. Hormonal induction of lactation should be practice only in infertile animals; it should not be followed as a routine practice, as an alternate to normal lactation. Estrogen and progesterone in 1:2.5 ratios is effective in exotic and cross bred while 1:1 ratio is effective in indigenous cows and buffaloes for artificial induction because of short luteal [42]. These methods of artificial induction of lactation yield 60 to 70% milk of previous lactation increasing.

The use of glucocorticoids close to when milking began, methods to boost prolactin production during the "lactogenic" phase of induction, the impact of the season, how various dairy ruminants responded to exogenous bST, and other changes were made in the following stages. Induction of animals that were unable to conceive as well as heifers that were younger than usual breeding age has also been compared [43,44]. Early testing of transgenic animals as potential mammary bioreactors can be accomplished by inducing lactation in young heifers. This short-term induced lactation scheme is still being modified.

Hormones have a significant impact on the growth and operation of the mammary gland, as demonstrated by numerous in vivo and in vitro investigations [18]. Studies looking at how estrogens affect the development of the mammary gland in dairy cows revealed that estrogen increases the growth of the mammary duct and that estrogen and progesterone together enhance the development of the mammary glands lobule-alveoli [34]. When cows give birth, estrogen also helps to start the lactogenesis process. Estrogen triggers lactation in two ways: first, it causes the anterior pituitary gland to release prolactin into the blood [45] second, it raises the proportion of prolactin receptors in mammary cells [46].

The high levels of progesterone during pregnancy help to regulate lobular-alveolar growth and inhibit lactogenesis, even though combinations of exogenous progesterone and estrogen interact synergistically to enhance lobular-alveolar growth. Lactogenesis is inhibited in multiple ways by progesterone. One illustration of this is how it inhibits the lactogenic activity of glucocorticoids by blocking glucocorticoid receptors in mammary tissues. Although the precise mechanism by which progesterone does this is unknown, the commencement of lactogenesis is enabled by the elimination of the progesterone block, luteolysis, and a fall in progesterone as parturition approaches [5].

The development of the mammary gland, which results in the differentiation of the gland's alveolar cells, is likewise influenced by glucocorticoids, with cortisol serving as the primary glucocorticoid in cattle. For binding sites on mammary epithelial cells, progesterone and glucocorticoids compete [47]. The increase in glucocorticoids displaces progesterone from mammary cell receptors, reducing the progesterone block to prolactin receptor synthesis, which helps in the induction of lactation in non-lactating cows with a developed mammary gland [5]. Prolactin supplementation can increase the amount of milk produced by these induced lactations, providing more proof that the hormones (estrogen, progesterone, prolactin, and glucocorticoids) interact synergistically to initiate lactogenesis [48].

Research is being done to find out how the hormones interact to increase lactogenesis as a result of the use of exogenous hormones to simulate mammary development during pregnancy. It was shown that induced lactations actually happened in treated animals during these attempts to simulate mammary development with different dosages of exogenous hormones. As a result of these findings, exogenous hormones are now used to induce lactations in non-pregnant cattle.

For more than 60 years, methods to lower culling rates and replacement costs by hormonally inducing lactation in dairy cattle have been tried with varying degrees of success [9]. By keeping animals that would otherwise be culled from the dairy herd, dairy producers would be able to reduce the number of nonbreeder cows lost to herd culling and lower replacement costs.

Buying replacement heifers vs inducing lactation in non-pregnant cows would be more profitable, according to Magliaro et al. [19]. A lactation-inducing estrogen/progesterone strategy was used on healthy, multiparous, non-pregnant cows. An annual stream of net revenues for induced animals and peer heifers was given a net present value (NPV) calculation. When comparing induced cows to replacement heifers, Magliaro et al. [19] and Kensinger [11] assessed the net present value (NPV) and discovered that the induced cows' NPV was $520 higher. In these calculations, the use of bovine somatotropin (bST) to initiate lactation in cows and increase milk production was also taken into account. It was projected that employing BST would provide a $261/cow mean annual NPV advantage.

Dairy producers may boost their profitability by encouraging non-pregnant cows to go into lactation if a similar approach were allowed by the FDA [19]. The use of steroids to stimulate lactation is currently prohibited due to worries about consumer safety and the presence of hormones in milk. Early methods for lactation induction involved long-term hormone treatment lasting 120 to 180 days, which had poor success rates and low milk production. After the first series of injections, 60% of the treated animals (6 of 9 cows and 1 heifer) were able to successfully initiate lactation using the 7-d injection protocol used by Smith and Schanbacher [9], which combined the hormones 17-estradiol (0.1 mg/kg BW/d) and progesterone (0.25 mg/kg BW/d).

Despite having a 40% failure rate, Smith and Schanbacher [9] were able to induce lactation in the majority of the animals using the shortened approach. Other researchers have the opportunity to look at protocols to increase the success rate of artificially inducing lactation in dairy cows that aren't pregnant or lactating because of this high failure rate. Exogenous dexamethasone [10,14,15] and/or reserpine (14,17,49] were frequently used in induction schemes in an effort to increase the success of the process (17,18,50]. Exogenous reserpine can mimic the substantial rise in prolactin found several days prepartum in pregnant cows [51] by causing a spike in blood prolactin concentration that lasts for several hours in cattle [52]. The administration of the synthetic glucocorticoid dexamethasone can imitate elevated glucocorticoid levels. It is also well known that plasma glucocorticoids drastically increase at the time of parturition in ruminant species (14,51,53].

Injections of estrogen alone or in combination with progesterone were used over an extended period of time to mimic pregnancy in ruminants. Complete mammary cell differentiation and development was also believed to require this long-term steroid stimulation [15,54]. Other researchers [17,50] hypothesized that a longer duration of treatment was required to improve success rates (the number of animals producing a defined milk yield) and to eliminate the variation in milk yields experienced using the 7-d treatment. Smith and Schanbacher [9] were able to disprove this theory using higher dosages of estrogen and progesterone injections for 7-d.

Increasing the injection period from 7-d to 11-d, or 12-d, as performed by Peel *et al.* [17] and Erb *et al.* [50] did not improve success rates (success > 1 kg/d within 24 after start of milking) or eliminate the variation in milk yields reported between animals induced into lactation. Lembowicz et al. (1978) were able to successfully reduce the 7-d estrogen and progesterone protocol to 5·5 d, or even 3·5 d, in multiparous Polish Black and White cows, so that its application would be more practical in commercial herds. In that study, doses of 17-β estradiol and progesterone, as outlined by Smith and Schanbacher (1973), were used in addition to eight single injections of reserpine on days 9 to 16 at a dose of 22·5 mg/cow/d. The benefits of this modified procedure included its simplicity and a decrease in estrus-like excitement (mounting), which would be advantageous to producers despite the lower milk yields it produced compared to cows induced into lactation with the 7-d treatment [49].

Researchers have looked at adding the exogenous synthetic glucocorticoid dexamethasone to induction methods since it is thought that the rise in circulating glucocorticoids at parturition is a crucial factor in starting lactogenesis [14]. By giving 3 separate injections of dexamethasone (20 mg/cow/d) to 6 heifers and 10 cows on days 18, 19, and 20 of the induction procedure, Collier and colleagues [14] modified the 7-d treatment recommended by Smith and Schanbacher [9]. Success in this trial was 69% (success > 9 kg milk/d at peak yield); however, it was determined that these results were comparable to those published by Smith and Schanbacher [9] and that dexamethasone did not significantly increase the success rate.

Using 19 dairy cows of different breeds and ages, Chakriyarat *et al.* [15] investigated the addition of 3 single injections of dexamethasone (0.028 mg/kg BW/d) on days 18, 19, and 20 of the 7-d estrogen-progesterone induction procedure. According to these researchers, adding dexamethasone injections enhanced the number of cows that were effectively induced into lactation (9 of 11; 82%) in comparison to cows who were successfully induced into lactation without dexamethasone (3 of 11; 27%) [15]. Eleven Holstein cows and 9 Guernsey cows were induced into lactation with 17-β estradiol (10 mg/kg BW/d) and progesterone (25 mg/kg BW/d) for 21 d, in addition to 3 single injections of dexamethasone (0.028 mg/kg BW/d) on days 31 to 34, again improving success rate (success > 5 kg milk/d) but not milk yields compared with cows not receiving dexamethasone injections (Fleming et al., 1986). These findings imply that although glucocorticoids do not appear to increase milk production, they may be crucial in triggering lactogenesis in the stimulated cow. The inclusion of reserpine injections, Collier and colleagues [14] pursued adjustments to the 7-d estrogen/progesterone protocol in an effort to increase success rates and reduce animal-to-animal variation in milk outputs. Prolactin was thought to be a limiting element of the "lactogenic complex" in cows that failed to produce milk after receiving a 7-d estrogen and progesterone therapy [10].

Cows who were not pregnant received injections of reserpine on either days 8, 10, and 14 of the trial, or on days 13, 14, 15, and 16. Days 13, 14, 15, and 16 were selected so that prolactin levels in induced cows would resemble the rise in prolactin seen in pregnant cows during the period just before parturition [10,51]. Based on findings from an earlier study that showed mammary tissue from induced cows was experiencing cellular changes associated with lactogenesis by day eight and continuing until day sixteen of treatment [10,55] reserpine was delivered on days eight, ten, eleven, and twelve.

Releasing prolactin with the aid of reserpine decreased the variation in milk production between individuals and increased the success rate (success > 9 kg milk/d at peak yield) from 40 to 100% in cows given reserpine on days 13 to 16, and from 75 to 100% in cows given reserpine injections on days 8, 10, 12, and 14 (Collier et al., 1977). Using mixed-breed dairy cows, Peel *et al.* [17] showed that supplementing the Smith and Schanbacher [19] 7-d protocol with reserpine (5 mg/d) on days 1, 6, 11, 16, and 21 did not increase milk yields, but did increase the proportion of cows responding to lactation induction treatment when compared to controls receiving only 17- estradiol and progesterone injections.

The 7-d estrogen and progesterone treatment protocol has undergone a number of modifications that have resulted in higher success rates (success defined by the scientist, but typically > 9 kg milk/d peak yield), but little progress has been reported in terms of reducing variation in milk yields among animals [10,15,17]. To keep raising the success rate, get rid of cow-to-cow variation in milk yields, and boost milk yields, more research is needed to create new procedures for inducing lactation.

Prostaglandin F2 administration removes the progesterone source (corpus luteum), induced cows may be more responsive to reserpine and dexamethasone treatment after the initial estrogen and progesterone protocol because progesterone and glucocorticoids compete for binding sites in mammary tissue [5]. Progesterone's inhibitory effect on lactogenesis is eliminated when glucocorticoids displace it from binding sites in breast tissue through the process of induced luteolysis [5]. Therefore, the ability to start a lactation induction program at very diverse points in the estrous cycle estrus and metestrus, when progesterone levels are low and estrogen levels are high, or diestrus, when progesterone is the dominating steroid hormone is made possible by the use of PGF2 to induce luteolysis. After the initial estrogen-progesterone therapy, exogenous PGF2 may be utilized to ensure luteolysis and reduce circulating progesterone at the time of glucocorticoid and reserpine delivery.

Use of prostaglandin F2α for estrous synchronization

Prostaglandin F2 (PGF2) administration has been demonstrated to cause luteolysis in the bovine [56,57]. In order to cause the corpus luteum (CL) to recede between days 5 and 16 of the estrous cycle in cattle, Rowson et al. (1972) injected 0.5 mg/d PGF2 on 2 consecutive days into the uterine horn ipsilateral to the CL.

PGF2 dosage and the stage of the estrous cycle at the time of administration have been studied, and results indicate that these factors have an impact on the estrous response. Low doses of PGF2 (5 and 10 mg) administered to beef heifers 13 to 14 months old and of mixed breed resulted in fewer heifers exhibiting estrus when given PGF2 in the early stage of the estrous cycle; however, as the stage of the estrous cycle at which heifers were treated advanced, the number of heifers exhibiting estrus increased. This was the finding of Berardinelli and Adair [58]. More heifers exhibited estrus during the first few days of the luteal phase (d 5 to 9 of the estrous cycle) when PGF2 was administered at higher doses (25 mg or 30 mg).

Cattle administered with either 17.5 mg or 25 mg of PGF2 had identical estrous responses and conception rates at the time of first service [59]. Other researchers [60-62] have demonstrated that giving PGF2 to dairy heifers and beef cattle between days five and nine of the estrous cycle results in fewer cows responding to treatment than giving PGF2 later in the estrous cycle (days twelve to eighteen).

All cows should be in the luteal phase of the estrous cycle and prepared to respond to a second PGF2 injection after 11 to 12 days. 30 randomly cycling Holstein heifers were given two injections of 30 mg PGF2 tromethamine salt (PGF2 tham salt) by King and Robertson in 1974 [63]. The injections were spaced 10 days apart. 25 of the 30 treated heifers (or 83%) were in estrus and became inseminated 2 to 4 days after the second PGF2 injection [63]. 40% of the inseminated heifers were found to be pregnant at 60 days after insemination. According to findings from related investigations, no animals given first PGF2 between days 0 and 4 of the estrous cycle showed any signs of estrus. Similar outcomes were reported by Burfening et al. (1978) using Hereford heifers that received two injections of PGF2-tham salt (33.4 mg), 11 days apart. However, only 71% of the treated heifers were seen in estrus after the second PGF2 injection.

Utilizing PGF2 gives a desirable way to control the estrous cycle stage and start lactation induction methods in cows with more comparable endocrine conditions. This may present a chance to lessen variation in the number of animals responding to lactation induction, as well as potential variation in milk supply.

Use of Bovine somatotropin: Bovine somatotropin (bST), commonly known as bovine growth hormone, is a naturally occurring protein that is secreted by the anterior pituitary gland [65]. According to Fesseha et al. [66], the circulating concentration of bST is positively connected with the development of the mammary gland and milk production. The use of bST enhances milk output in nursing cattle by improving the availability and utilization of nutrients for milk synthesis [67]. bST controls the partitioning of nutrients in lactation cattle. Recombinant bST (rbST), a version permitted for use on dairy cows, was created in 1979 and its usage was authorized in the USA in 1993 [68]. Since then, a large body of research in temperate regions has demonstrated that rbST increases milk production and feed efficiency in lactating cows by St-Pierre et al. [69], despite reports of variable magnitude of responses in cattle treated with rbST [68,70), for which it has been identified that management factors are important sources of variation [71].

The administration of rbST to dairy cows boosted milk output by 4.0 kg/day without having a negative impact on the cows' health, according to a meta-analysis of 26 studies on the effect of rbST [69]. Primiparous cows produced less milk after receiving rbST treatment than multiparous cows did [72,91]. This is because primiparous cows are still growing, and even though they have higher levels of endogenous bST than multiparous, the nutrients are still being distributed to meet both growth requirements and requirements for milk synthesis [74]. On the other hand, it is well recognized that increased nutritional needs, particularly for energy, are brought on by milk production. As a result, the cow must use her body reserves to continue milk production when these needs are not met, which degrades body condition [75]. According to some research, cows treated with rbST maintain their body condition compared to untreated cows, but according to others, they lose it [76,77]. Loss of body weight or physical condition in Lactation cows may have an adverse influence on the amount of milk they produce [78].

The use of rbST for dairy cattle in tropical climates has received little attention. Sesame oil and zinc (ZSO-rbST) or lecithin and vitamin E (VEL-rbST) are the two commercial rbST somatotropin products that are currently being used in Latin America. Both of these products provide rbST but differ in the vehicle component they utilize. Contrary to the substantial study conducted in North America, there is little information from studies conducted in tropical regions analyzing the impact of various commercial somatotropin formulations on milk production.

Additionally, it has been demonstrated that cold or hot temperatures negatively affect the rbST response, with periods of heat stress producing lower responses in milk production than those under moderate climatic circumstances [79]. The findings of studies involving Holstein cows using two distinct rbST formulations at industrial farms in Brazil were incongruous in terms of their ability to produce. Almeida and Viechnieski [80] reported that cows treated with VEL-rbST produced more milk (+ 1.6 kg/day) than cows treated with ZSO-rbST, while De Morais et al. (2017) reported that cows treated with Z-rbST produced more milk (+ 1.3 kg/day) than cows treated with VEL-rbST. Similar to this, Vargas et al. [81] observed that the use of VEL-rbST increased milk output in cross-bred cow pasture management in Colombia. It is challenging to duplicate the results for all the realities that exist in the region because of these disparities, which may be caused by a variety of factors including environment, management, nutrition, and genetic potential of cattle that exist throughout Latin America. Two commercial rbST formulations are available to dairy farmers in Peru, however there is no local research assessing their efficacy. Dairy farmers could utilize this information to make an informed decision on the rbST formulation that will increase their herds' profitability and milk production.

Bovine somatotropin augmented milk yields in cows hormonally induced into lactation much like that observed in postpartum animals [52]. The response to bST increased over the 70-d treatment period.

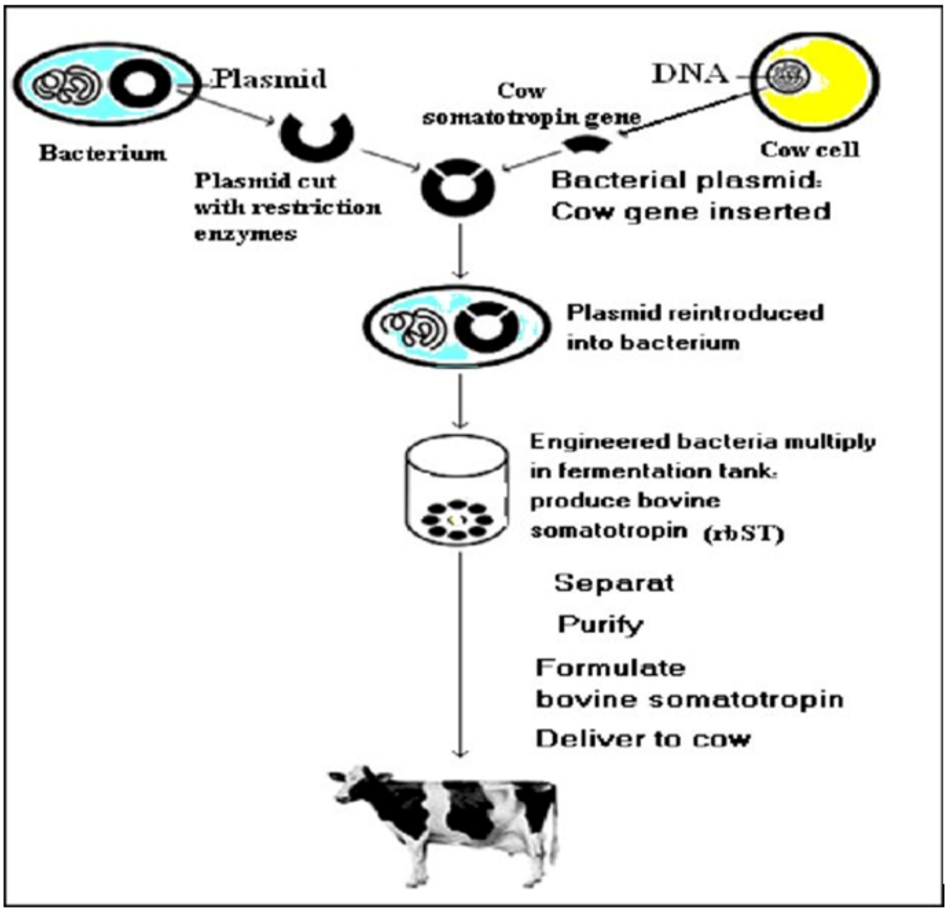

Figure 1. Bovine somatotropin production

Historical use of Bovine somatotropin: According to Asimov and Krouze (1937), they were the first scientists to show that giving dairy cows injections of raw pituitary extracts from cattle boosted their milk production. The four treatment groups, which all received the same dosage of pituitary extract, saw an average increase in milk yield of 11 L. Li et al. (1945) isolated somatotropin (ST) from an ox anterior pituitary by treating the fresh anterior pituitary substance or acetone-dried glands with cysteine, which destroys lactogenic, thyrotropic, and gonadotropic activities but not growth potency. Young (1947) confirmed the conclusions of Asmimov and Krouse (1937) and showed that ST was the galactopoietic agent in pituitary extracts that promoted milk supply in dairy cows. Although studies showed that bovine pituitary extracts could increase milk yields, the quantity of bovine pituitary extract required to conduct extensive studies was constrained because only small amounts of bovine somatotropin (bST) could be purified from each pituitary gland (5 to 15 mg). Pituitary-derived bST is not widely available, so studies could only include a small number of cows given short-term treatment [12].

The development of gene splicing in genetic engineering throughout the 1970s made it possible to take DNA from one species and insert it into another. It is possible to splice the bST gene from the bovine pituitary gland into the plasmid (a short circular piece of DNA) of an Escherichia coli K-12 bacteria. Following the bacterium's death and the separation and purification of bST in large numbers, the E. coli cells will produce the new protein that is coded for bST. The first study contrasting a 6-day administration of naturally occurring bST (25 mg/d) and recombinant-derived bST (rbST) (25 mg/d) to dairy cows was conducted in 1982 as a result of these advancements in DNA technology. Milk yields from 12 Holstein cows (92 ± 20 DIM) given 25 mg/d of rbST increased by 12.9%, and yields from cows given 25 mg/d of natural bST increased by 10.3%, showing that recombinant derived bST was just as effective as pituitary derived bST in increasing milk yield. Research utilizing this protein has significantly grown since the creation of rbST.

Mass production and use of rbST: Long-term studies could be conducted and assessed thanks to the widespread manufacture of rbST. The lactational performance of 30 Holstein cows in their second to fifth lactation was studied by Bauman et al. (1985) starting at 84± 10 d postpartum using long-term (188 d) daily dose of either rbST or pituitary generated bST. Cows treated with pituitary-derived bST (13.5, 27, or 40 to 50 mg/d) showed a milk yield increase of 16% while cows treated with rbST (13.5, 27 or 40 to 50 mg/d) had an increase in milk yield of 23 to 41% above control cows. Additionally, Bauman et al. (1985) noted that a reduction in energy balance was brought on by the increased milk output brought on by the administration of somatotropin. In order to make up for the decline in energy balance, voluntary feed intake rose as rbST dose was raised. In comparison to control cows, treatment cows' net energy intake increased to 35.1 Mcal/d (natural bST 27 mg/d), 36.1 Mcal/d (rbST 13.5 mg/d), 39.2 Mcal/d (rbST 27 mg/d), and 37.5 Mcal/d (rbST 40.5 mg/d), respectively, from 34.1 Mcal/d. By the tenth week of treatment, all treated cows had a positive energy balance.

Even though Bauman *et al.* (1985) were able to show that rbST was just as effective as pituitary-derived bST and continued to increase milk production during long-term administration (188 d), more research was required to examine the utilization of a prolonged-release formulation. A effective prolonged-release formulation was thought to be able to do away with the requirement for rbST injections every day, saving money and labor. 60± 3 d postpartum, a prolonged-release formulation containing 500 mg of rbST was given to 80 Holstein cows in their first, second, or third lactation at 14-d intervals. However, a cyclic pattern in milk yield was seen within each 14-d injection interval because the formulation provided a diminishing amount of rbST during the last one-third of the injection interval. The prolonged-release formulation was successful in increasing fat corrected milk yields by 11.4%. Cows receiving rbST increased voluntary feed intake as previously reported (Bauman *et al.,* 1985), with a mean net energy intake of 31.8 Mcal/d for treated cows and 30.2 Mcal/d for control cows. Similar findings have been reported by other researchers [50] employing a prolonged-release system of N-methionyl bovine somatotropin (Sometribove, Monsanto Company, St. Louis, MO) with 14-d injection intervals.

Current situation of bST: When milking, prolactin is released when the udder and teats are stimulated (by massage, for example). After the onset of lactation, prolactin is no longer necessary for milk production. The growth hormone bSTr, also known as bovine somatotropin, is utilized to improve milk output.

It is difficult to emphasize the importance of the effects of growth hormone (GH) on milk supply and mammary development (mammogenesis) [8]. Undoubtedly, the availability of bST through recombinant DNA technology and the extensively researched benefits of exogenous bST on milk production and the mobilization of nutrients to support increased milk production in cows, goats, sheep, and camels are major contributors to the interest in GH in the past 30 years or so.

According to Bauman and Currie (1980), studies [12] and publications show that bST is still the most thoroughly tested and researched recombinant DNA-derived product ever created for use in dairy ruminants. It is unclear how attitudes of companies toward the development of products to increase growth or lactation responses will fare in the future given the market and consumer forces that limit use of bST in the United States and Western Europe, despite stringent safety assurances and Food and Drug Administration approval in 1994. The discussion over the authorization and subsequent use of bST in dairy cows was heated for a variety of reasons, [38]. However, this requires the use of exogenous therapy with GH-releasing factor [30]. It is feasible to boost native GH secretion and the corresponding increases in milk production. It's noteworthy that Russian researchers Asimov and Krouze (1999) carried out one of the earliest large-scale demonstrations of GH's (in this case This seems out of this planet in the political climate of today. In fact, current societal conditions show that the general public lacks confidence in science and scientific principles, which is bad news for our citizens' and citizen-leaders' ability to make logical, well-informed decisions. This holds true whether the problems are related to recombinant protein use and mammary development, genetically engineered plants and animals, or the occurrence and causes of climate change.

Recombinant bovine somatotropin on milk production: The increase in milk production observed in primiparous and multiparous cows of the VEL-rbST group with respect to the control is within the range of an increase of 3–5 kg/day reported by other researchers [69]. As indicated by Bauman [52], the use of rbST induces an increase in the blood concentration of growth hormone and insulin-like growth factor (IGF-1) which improves milk production mainly through greater lipolysis and prioritization of nutrients toward the mammary gland. However, a higher effect on milk production is observed in multiparous than primiparous cows treated with rbST which was evidenced by previous studies.

The explanation is that even though primiparous cows could have more endogenous bST than multiparous cows, during the first lactation cows continue growing and the nutrients are distributed to cover growth requirements and milk production [74]. In this sense, the growth stage of primiparous cows would reduce the increases in milk production induced by rbST. In primiparous and multiparous cows, no significant differences were found between evaluated rbST, which is similar to that indicated by Posada et al. [73], Barrios [84]. and Flores et al. [85]. On the other hand, Almeida and Viechnieski [80] reported significant differences between rbST, where cows injected with VEL-rbST produced 1.6 kg/day more milk than those treated with ZSO-rbST, while De Morais *et al.* (2017) reported differences between ZSO-rbST and VEL-rbST, being higher for primiparous (+ 2 kg/day) and multiparous cows (+ 1.3 kg/day) treated with ZSO-rbST. These two results are different from those obtained in the present study and may be attributable to differences in general management conditions that are difficult to detect, which is one of the main sources of variation in the response of dairy cows to rbST [71].

In the case of primiparous cows, the results are similar to those reported by Barrios [84] but differ from the data of De Morais *et al.* (2017) who indicate a higher milk production for cows with ZSO-rbST than with VEL-rbST in 6 of 17 injection cycles. On the other hand, in multiparas, the results of this study agree with those of Almeida and Viechnieski [80] who reported that milk production of multiparous cows with VEL-rbST was statistically higher than other commercial rbST in all the cycles evaluated but differ from De Morais et al. (2017) who reported that the milk production of cows with rbST was higher in cows with ZSO-rbST. From the present review, it is observed that the milk production response to rbST of primiparous cows is more evident than for multiparous cows but the nature of this study does not explain that difference in response.

In relation to the evaluation of the rbST response on milk production in the 14 days of the 12 injection cycles, rbST formulations were not different in primiparous or multiparas, unlike De Morais et al. (2017) who report that in primiparous the group with ZSO-rbST was greater than VEL-rbST in 9 days of the cycle, while in multiparous primiparous, it was greater in 8 days. In the present study, it is observed that the difference in production was observed in the first half of the application cycle in relation to what was obtained in the rest of the days. This is similar to what was found by De Morais et al. (2017), who detailed that the highest production of the treatment with ZSO-rbST was concentrated between days 3 and 9 of the injection cycle and for VEL-rbST, between days 2 and 8. Figures 4 and 5 show that differences were found between primiparous cows treated with VEL-rbST and the control on days 2, 3, 4, 5, 6, 7, and 8, while in multiparous cows, the differences were on days 1, 2, 4, 5, 6, 7, and 8. For days 9 to 14, there was no significant difference between treatments which is consistent with what was observed by Bauman et al. (1989) who reported peak production at day 7 of the cycle.

There are numerous studies that show increases in IGF-1 production explain the improvement of milk production in cows treated with various formulations of rbST (86; 87; 88; 89 ; 90) without definition if differences are related to the rbST vehicle. In this review, the results of milk production could indicate that the impact of the vehicle on the release profile of rbST from VEL-rbST could be better than ZSO-rbST due to the higher milk production in 8 of the 14 days of the injection cycle in both primiparous and multiparous cows.

The rbST formulations had no significant effect on the body condition of the cows as reported by Posada *et al.* [90] and De Morais *et al.* (2017). Unlike other studies where body condition is reduced [76,77], in this review, the results could be due to the fact that the animals started the with more than 10 weeks of lactation on average exceeding the first 8 weeks postpartum which are critical for negative energy balance. Another possible explanation of the maintenance of body condition in this review may be due to the increase in voluntary feed consumption, which although not measured during the test, different studies have reported an increase in feed consumption in animals that were administered rbST [91,69]. This in turn serves to cover the requirements of the additional milk production without compromising body condition.

Effect of rbST on milk production: A significant effect of parity was observed on milk production [92]. Significant differences were also observed between the group of cows from the control group and the cows with VEL-rbST but not between VEL-rbST and ZSO-rbST in both primiparous and multiparous cows (Figure 2). In primiparous cows, the average milk production in the control group, ZSO-rbST, and VEL-rbST was 35.2, 37.1, and 38.2 kg/day while in multiparous cows, it was 39.9, 41.6, and 43.1 kg/, respectively. For primiparous cows, the difference in milk production between the VEL-rbST and control groups was 3 kg/day while in multiparous cows, it was 3.2 kg/day for VEL-rbST.

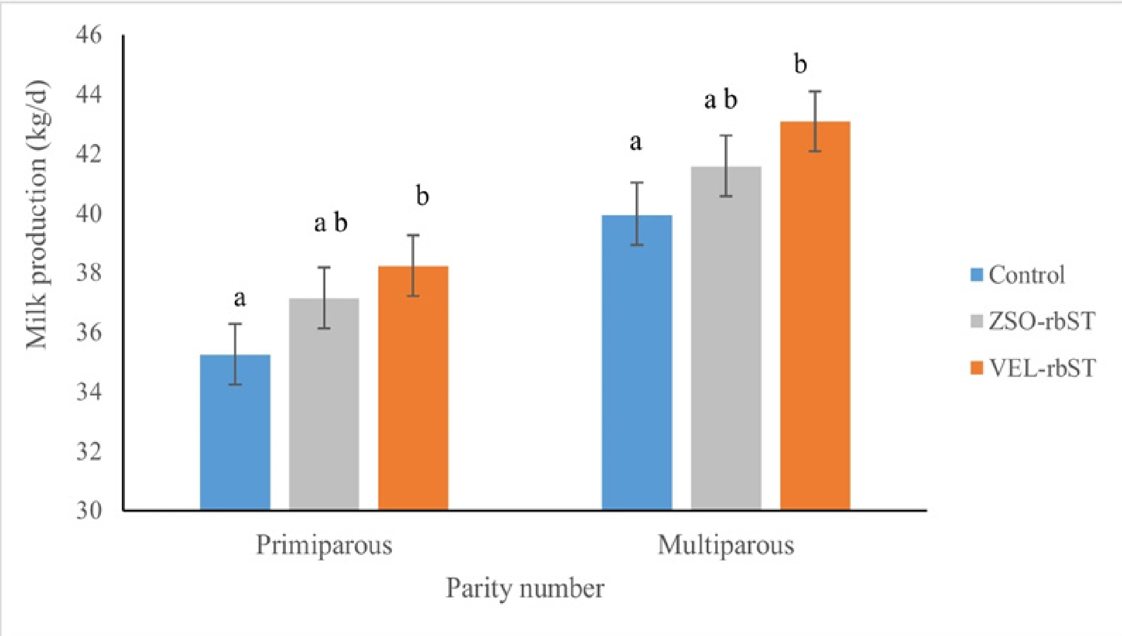

Figure 2. Effect of two formulations of recombinant bovine somatotropin on milk production and body condition of cattle under intensive management

In primiparous cows, differences in milk production were found in the 12 cycles between cows treated with rbST and the control but not between rbST formulations ((Figure 3), while in multiparous cows, no differences were found between ZSO-rbST and the control , or between rbST formulations ($p > 0.05$) but differences were found between multiparous cows treated with VEL-rbST . In primiparous cows, the average milk production in the control, ZSO-rbST, and VEL-rbST cows was 34.7, 37.9, and 38.2 kg/day while in multiparous cows; they were 40.2, 41.6, and 42.7 kg/day respectively.

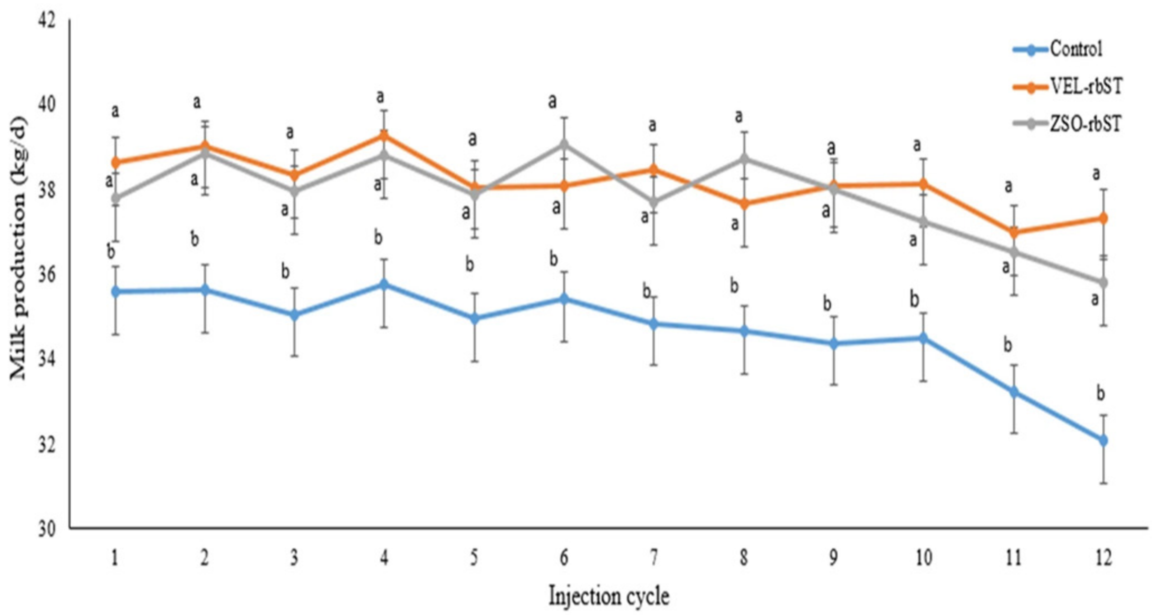

Figure 3. Average milk production within a cycle with different letters (a–b) is significantly different, Sources:(Gómez,*et al.,*2022).

Milk production (kg/day) of primiparous and multiparous cows treated with rbST (VEL-rbST or ZSO-rbST) or untreated (control) cows during the entire 168 days recorded in Figure 3. Average milk production within each group by parity with different letters (a–b) are shows the different (Gómez,*et al.,*2022).

Days in milk during use of rbST's: Days in milk (DIM) is related closely to dry period length and is a good indicator of reproductive efficiency and herd management. The 12-month average for DIM should be 160 to 170 days.Higher doses resulted in more days open and a lower pregnancy rate, according to studies looking at the administration of rbST during early lactation (28 DIM) at dose rates of 0, 12.5, 25, and 40 to 50 mg/d [70,93]. Eppard et al. [94] observed that days open and services per conception were equivalent to controls after administering rbST starting at 84 DIM at doses of 0, 13.5, 27, and 40.5 mg/d. As a result, rbST's detrimental effects on reproductive function may be explained by its capacity to worsen the energy balance of early lactation cows (84 DIM) that are already in a negative energy balance [95]. However, because these cows are in positive energy balance and often start lactation at modest levels of milk output, delivering rbST at the start of lactation to non-pregnant, non-lactating cows induced into lactation shouldn't have a negative impact on reproductive performance.

It has also been attempted to administer various doses of rbST at 96 ±7 days in milk (DIM) at intervals of 4 weeks using a sustained-delivery device. In a sustained-release vehicle, three different doses of rbST (320, 640, and 960 mg) were delivered by Oldenbroek *et al.* [96] at intervals of 28 days. With a 19% increase in milk energy output in weeks 13 to 36, it was discovered that the 640 mg dose of bST had the best effects. Another study conducted by Leonard et al. [63] examining a 28-d sustained-release formulation given to cows in early, mid, and late lactation also included dosages of 320, 640, and 960 mg of rbST and investigated the effect of giving the formulation to cows during two consecutive lactations. Injections of rbST increased milk production over the course of two successive lactations, while the 28-day slow-release formulation only increased milk production over the course of three weeks, giving cows one week to correct their negative energy balance during the first lactation [63].

All cows receiving somatotropin increased voluntary feed intake to make up for the extra nutrients needed for enhanced milk supply, as was shown in prior studies looking at the administration of rbST [83].

Induced cows attained peak milk production of 32.2 ± 11.5 kg/d at 125 ± 47 d of lactation. Whereas induced cows required more days to attain peak lactation than postpartum cows, duration of lactation was normal; as induced cows averaged 289 ± 74 DIM [19].

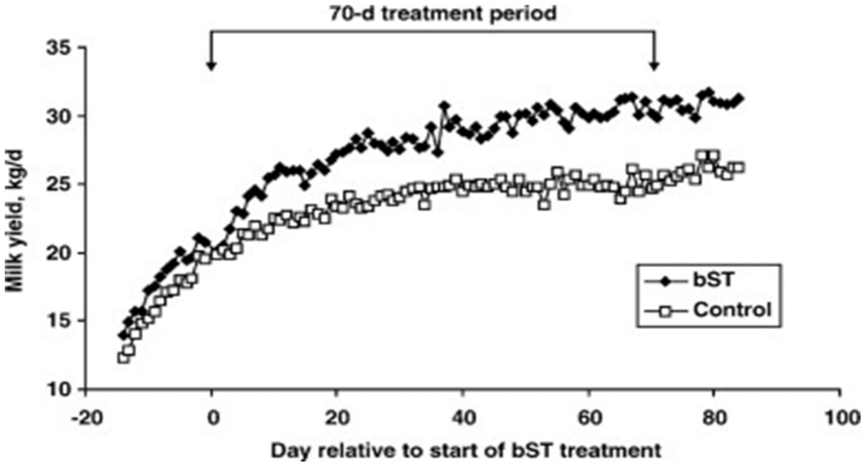

Figure 4. Comparison of milk yields of cows induced into lactation and treated with bST with induced cows not treated with bST (control). Sources: [19].

Milk yield and composition of cows untreated and treated with rbST: The impact of rbST usage on milk composition has been the subject of numerous investigations. If treated cows were in a negative energy balance while undergoing bST therapy, Bauman et al. (1989) found that the fat content of milk increased with rbST treatment (given 60 ±3 DIM). When voluntarily increased feed intake and a positive energy balance are established, milk fat content is comparable to that of untreated cows. According to Barbano et al. (1992), the mean percentages of lactose, fat, total solids, SNF, casein, and true protein in milk from control and rbST-treated cows during the treatment period (wk 2 to 41 of lactation) were comparable. In addition, Hartnell et al. [83] came to the conclusion that rbST administration had no effect on the somatic cell count (SCC), milk fat, protein, lactose, ash, calcium, or phosphorus concentrations, or any of the other milk constituents. The use of rbST does not change the composition of milk, according to reports from other researchers [30].

Bovine somatotropin (bST) is a natural metabolic protein hormone produced by the pituitary gland in all cattle and used to increase milk production in dairy cows (FAO, 2013). Recombinant bovine somatotropins (rbST), that has several amino acids, have been synthesized using recombinant DNA techniques. rBST is administered subcutaneously at day 60 of a cow's lactation cycle when milk production normally begins to decrease and repeated every 14 days. Even though bST has the potential to increase the efficiency of milk production, there is no change in milk composition. In the case of rBST, potentially 10-15% more milk can be obtained from each cow. rBST is biologically inactive in humans and its residues in food products have no physiological effect.

Concentration of Insulin-growth factor-I (IGF-1) is no significant difference in bovine growth hormone levels in milk from rBGH-treated and untreated cows. Even if there were a much higher level of bovine growth hormone ingested by humans, our digestive system would break down and inactivate the hormone protein. In addition, the bovine growth hormone does not affect human growth hormone receptors and good management measures should be taken as per manufacturer to ensure a high response in milk yield to bST administration. Thus, the use of rbST to improve productivity within the lactating cow herd allows for a reduction in resource use and environmental impact per unit of milk shown in Table 2.

Table 2. Comparing milk yield and composition of cows untreated and treated with rbST

Species	Groups of treatment	Milk yield(L/day)	Protein	Fate	Lactose	References
Cattle	Control	23.5	3.65	4.29	9	Kim and kim, 2012
	rbST	27.7	3.30	3.84	8.89	
Cattle	Control	20.7	3.16	3.50	4.51	Campos, *et al.*, 2011
	rbST	22.6	3.16	3.52	4.49	
Cattle	Control	15.6	3.27	3.67	-	Macina, *et al.,* 2011
	rbST	17.9	3.28	3.65	-	
Cattle	Control	41.9	2.86	3.30	-	Liboni, *et al.,* 2008
	rbST	45.6	2.81	3.82	-	
Cattle	Control	36.1	2.90	3.82	-	Liboni, *et al.*, 2008
	rbST	37.6	2.83	3.78	-	
Cattle	Control	12.9	3.45	3.94	4.90	Chaiyaboutr, et al., 2007
	rbST	14.6	3.51	4.62	4.62	

On average, 85% of the animals who underwent artificial induction of lactation succeeded, with 16 cows in group 1 (80%) and 18 cows in group 2 (90%). Artificial induction was judged successful if milk production exceeded 9 kg per day. Compared to Mellado et al. (2006), who claimed a 100% success rate, the success rate was lower. The hormone dosages were larger in this particular trial, which might have had an impact on the success rate. Animals from group 2 produced more milk on average than those from group 1 during the course of 324 lactation days) (Table 3). Animals in groups 1 and 2 produced milk on average of 6,137 kg and 7,103 kg, respectively, which amounted to 66.7% and 77.2% of the previous lactation. When compared to the 82% reported by Smith and Schanbacher (1973) [9], the percentage associated with the prior lactation that was seen was lower.

Table 3. The average milk production and composition of cows that received two different artificial inductions of lactation protocols.

milk production in kg	**Group one**	**Group two**	**P**	**CV%**
Fate correct	18.9±11.5	21.9±12.0	0.03	38.4
Milk 3.5%	17.6±10.6	20.2±12.4	0.04	38.2
Fate %	3.7±1.2	3.6±1.0	0.98	28.2
Protein %	3.3±0.5	3.3±0.5	0.98	11.6
Lactose%	4.3±0.5	4.4±0.5	0.98	9.2
Total solids %	12.3±1.3	12.2±1.2	0.98	9.1
Somatic cell count	384.9±781.7	523.4±1092.4	0.98	34.1

Sources Mellado *et al.* (2006),

Once all medications and dosages were identical for both artificial inductions of lactation protocols, the differences between the two groups were likely due to the dose and type of estradiol used in group 2. Estrogen and progesterone are crucial for the process of final growth of mammary gland ducts as well as the development of the lobular-alveolar structure, and it is likely that the higher dose of estradiol in group 2 caused a stronger synergism with progesterone.

Environmental impact the use of rbST: The use of rbST to improve productivity within the lactating cow herd allows for a reduction in resource use and environmental impact per unit of milk [67,69]. When evaluated a dairy herd of one million lactating cows supplemented with rbST and calculated the environmental impacts associated with producing the same amount of milk in a herd not supplemented with rbST. The herd supplemented with rBST required 11.8% fewer animals, used 8.5% less feed, 8.1% less cropping land and 8.1% less water. Moreover, the rBST herd produced 9% less nitrogen and 9.5% phosphorus in excreta and 8.1% fewer greenhouse gases. The use of rBST (reduced by nutrient partitioning) in dairy cattle has resulted in an average increase in daily milk yield of 4.5 kg per cow. This technology allows each cow to produce an average of 15% additional milk, resulting in one cow less producing manure, consuming feed and water, using electricity for milking and requiring human efforts for husbandry [97,67].

Livestock metabolism-use of rBST in lactating cows decreases the quantity of energy and protein needed, as well as the total feedstuff used. This reduces fossil fuel consumption and global warming potential. When conventional, conventional with rBST, and organic dairy operations are compared, 8% fewer cows are needed in an rBST-supplemented population, whereas organic production systems require a 25% increase. This is due to a lower milk yield per cow due to the pasture-based system, which requires greater maintenance energy expenditure associated with grazing behavior [91,98,99].

Use of Dexamethasone Trimethylacetate

Dexamethasone trimethylacetate injections started lactation in Ayrshire heifers after a series of injections of oestradiol benzoate with progesterone. After 20 mg/day for three days, lactation was normal, but 40 mg/day for four days caused a decrease in milk-like fluid with a high fat content [100]. Milk production was higher in induced-lactation heifers that received DEX than in control heifers from d 2 to 15 indicated Figure 5 below. Milk yields were similar thereafter until 305 DIM; with greater yields for 18-mo-old animals through 305 DIM. Time to peak production averaged 160 d, but heifers induced at 18 mo had higher peak yields than those induced at 14 mo. (22.9 kg/d; Table4).

Table 4. Effect of age at induction and dexamethasone (DEX) administration on 305-d yield and composition of milk from heifers induced into lactation

Component/Day	Age at induction		Treatment	
	14 mo	18 mo	DEX	Control
Milk yield, kg/d	17.4	18.9	18.2	18.2
Peak milk yield, kg/d	22.9	26.1	24.4	24.5
Days to peak milk yield	162	159	164	157
Fat, %	3.92	4.10	4.15	3.87
Protein, %	3.45	3.40	3.48	3.37
DIM	321	301	306	316

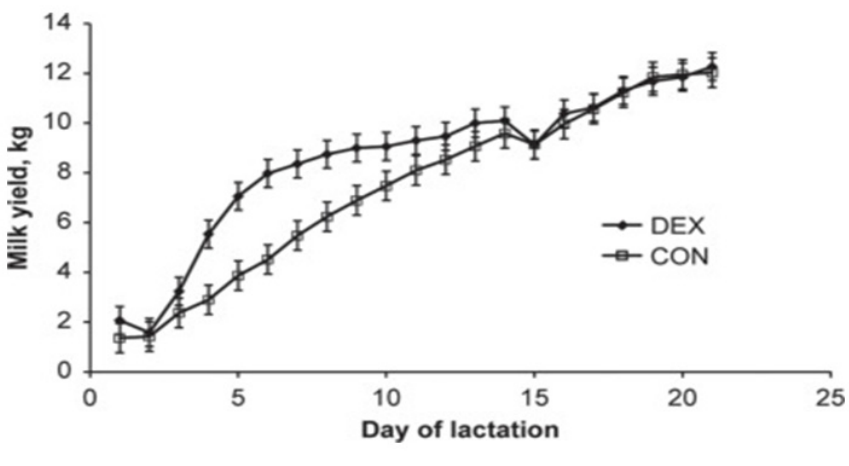

Figure 5. Comparison of initial milk yields of heifers induced into lactation and treated with 10 mg of dexamethasone (DEX) on d 1 and 2 of lactation with induced heifers not treated with dexamethasone (CON). Sources: [101].

At days 1 through 21 of lactation (4.51%), the study indicated that DEX heifers had a greater milk fat content than control heifers. Both groups' milk fat percentages stayed the same until day 305 and were comparable by day 14. Due to DEX therapy or age at induction, milk protein and lactose percentages were not altered. (Tables 5). Protein content decreased from 14.41% to 3.73% during the first 21 days of lactation (Tables 5), while lactose percentage increased from 2.72 to 5.09%. Somatic cell count decreased more rapidly in DEX-treated heifers, but no differences were observed due to age [44].

Table 5. Effect of age at induction and dexamethasone (DEX) administration on initial composition of milk from heifers induced into lactation

Component/Day	Age at induction		Treatment	
	14 mo	18 mo	DEX	Control
Fate,%				
1	2.74	1.69	2.76	1.66
3	3.65	2.91	3.86	2.70
5	4.63	4.36	5.56	3.43
7	4.79	5.25	5.80	4.24
14	4.34	4.85	4.70	4.49
21	4.03	4.48	4.28	4.24
Protein, %				
1	12.36	16.46	14.98	13.84
3	6.70	7.46	6.80	7.35
5	4.81	5.45	4.54	5.72
7	4.17	4.73	3.94	4.95
14	3.77	4.04	3.58	4.23
21	3.60	3.86	3.46	4.00
Lactose, %				
1	2.76	2.68	2.72	2.72
3	3.87	3.96	4.15	3.68
5	4.31	4.39	4.47	4.23
7	4.64	4.54	4.73	4.45
14	5.07	4.97	5.15	4.90
21	5.11	5.07	5.19	4.99
SCC, ×1,000 cells/mL				
1	5,879	5,819	8,111	3,587
3	4,230	3,845	6,211	1,863
5	1,486	1,111	1,650	946
7	843	555	716	682
14	295	468	562	201
21	494	84	180	397
IgG, mg/mL				
1	85.3	129.5	104.9	109.9
3	34.4	43.5	38.6	39.3
5	3.8	12.5	2.9	13.4
7	2.2	7.7	1.9	8.0
IgG, g				
1	79.9	103.4	90.5	92.8
3	47.8	66.9	61.4	53.3
5	16.3	30.5	18.4	28.4
7	15.3	25.1	14.6	25.8

According to Macrina *et al.* [44], the mean milk IgG content decreased from day 1 to day 7 and was higher for 18-month-old heifers compared to 14-month-old ones, but not mass. IgG concentration, mass, or the pace of reduction over time were unaffected by DEX treatment. Body weights for heifers who were induced at 14 mo and 580 34 kg (24 mo) of age at 6 months after lactation induction averaged 510 50 kg and 580 34 kg, respectively. Heifers induced at 14 months of age had a mean BW of 577 35 kg at 24 months of age. Induction of parturition in dairy herds can shorten the gestation period of cows while improving reproductive performance and management. Costs associated with induced cows and losses in lactation and calf production must be considered [44].

Table 6: The proportion of cows induced to calve and untreated cows which were observed to have retained fetal membranes

Parameters	**Retained fetal membranes**		
Herds not using prostagiaglandin	No	Yes	%
Untreated	168	8	4.6
Induced	326	64	16.4
Herds using prostaglandin			
Untreated	414	10	2.3
Induced with DexTMA only	584	135	18.8
Induced with DexTMA+prostagiandin	261	79	23.2

Sources (Mansell, *et al.*, 2006)

Table 7: Milk and fat production of cows induced to calve at various stages of pregnancy.

Months pregnant at time of induction	**Number of cows**	**Milk (liters)**	**Fat (kg)**
6.5	64	4769 ± 817	202 ± 31
7.0	114	4662 ± 1164	198 ± 46
7.5	200	4567 ± 922	197 ± 38
8.0	182	4621 ± 961	202 ± 39
8.5	12	4881 ± 1013	191 ± 37
Untreated cows	338	4805 ± 1103	206 ± 45

Sources (Mansell, *et al.*, 2006)

Six of the 1449 induced cows died during the first two weeks following calving, making induced animals determined to have more health issues than non-induced cows. At the end of 1992, there were about the same numbers of induced and untreated cows still in the herd [101]. In 28 of the 1449 induced cows (1.9%), owners reported lactation failure or low output. According to production data for the ensuing lactation, induced cows produced less milk than non-induced cows (4631 976 vs. 4805 1103 liters, n = 574). Induced cows produced less fat than control cows (199.3 39.3 kg vs. 206.1 44.8 kg, respectively). The amount of milk produced during the ensuing lactation was not significantly impacted by the stage of pregnancy at which induction was performed. (Table 7).

Milk Yield, Quality and Biochemical Profile in Artificial Induced Lactation Cows

Milk yield and quality with artificial induction of lactation: The variations in milk contents (fat, protein, and lactose) between induced and natural lactation in heifers (responders) were minimal. The somatic cell count (SCC) and milk composition did not change as a result of the artificial induction of lactation protocols [102]. According to Magliaro et al. [19], milk production in induced cows has fluctuated, averaging between 63 and 106% of the best lactation before.

When compared to non-synchronized heifers, the milk yield was considerably higher in pre-synchronized heifers with PGF2 (0.25 mg). Increased yield in pre-synchronized animals may be due to uniform follicle growth after luteolysis in conjunction with metoclopramide medication.

Total 122-day yields of actual milk (2966, 2729 kg), 3.5% Fat-corrected milk (FCM) (3077, 2964 kg), and 4.0%) solids-corrected milk (SCM) (2875, 2722 kg) did not differ between seasons. Daily yield per cow averaged 25.0 kg milk, 27.6 kg FCM, and 25.5 kg SCM. Milk composition did not differ between FEB and JUN cows Magliaro et al. [19]. Milk was discarded from day 0 to day 28 of the study (day 1-14 of lactation). Milk samples were collected from all three milking's on day 7, 14, 21, 28, 56, 84, and 112 of lactation, preserved with 2-bromo-2-nitropropane-l,3diol, and analyzed within two days for fat, total protein, lactose, and somatic cells (Table 8).

Table 8: Yield and composition of milk from Holstein reproductive culls induced to lactate in late winter (FEB) and early summer (JUN)

Parameters	FEB	Jun
Milk yield total(kg)	2,966	2,729
% Fat-corrected milk (FCM)	3,077	2,964
solids-corrected milk (SCM)	2,875	2,722
Milk yield total(kg/day)	25.3	24.7
% Fat-corrected milk (FCM)	27.4	27.7
solids-corrected milk (SCM)	25.6	25.4
Milk composition (kg/day)		
Fate %	4.0	4.5
Protein %	3.5	3.4
Lactose %	4.9	4.9
Somatic cells (10^3 /ml)	159	141

Induction was successful in 13 of 15 of FEB cows (86.7%) and 15 of 18 JUN cows (83.3%). The shape of the lactation curve was similar for both seasons with cows attaining a plateau (about 30 kg of milk/day) by week eight of lactation. Milk yield and composition did not significantly differ between seasons (Table 8). Furthermore, the results also showed that about 70% of the cows treated using this embodiment surprisingly produced more than 60 lbs. of milk/day and at times averaged production of over 70 lbs. of milk/day. Surprisingly, the cows' milk yield was not affected by season [19]. Regardless of the season of induction, adjusted milk yields (305ME) of the induced cows averaged 65% of their 305ME from the previous lactation (Table 9).

Table 9: Adjusted milk yield (305ME) of Holstein reproductive culls during either their induced lactation or after a previous calving

Season	Previous yield (kg)	Induced	
		Yield (kg)	% of previous yield
FEB	13,257	8,329	62.8
JUN	12,065	8004	66.3

Biochemical profile in artificial induced lactation of cows: Dairy cattle suffer a significant economic loss as a result of the disposal of animals owing to reproductive failures, and one of the main causes of this is a non-pregnant cow towards the conclusion of lactation. A technique used to replicate the last trimester of pregnancy and encourage the production of milk is known as artificial induction of lactation. This strategy offers owners a great alternative for maintaining a herd with good milk production potential and superior genetics, avoiding unproductive animals in the herd, creating new opportunities for reproduction, and increasing profits [19,33].

The use of lactation induction procedures has been reported for more than 60 years, including the use of hormones to induce lactation in heifers in the 1940s (Walker and Stanley, 1941). According to Freitas et al. [33], the duration of the hormone induction was too long and caused the animals to experience pain and discomfort. The regimen was eventually shortened to seven days as a result of a study by Smith and Schanbacher [9], which found that the cows produced 70% of their regular lactation's worth of milk. Although there is a lot of variation in the milk induction response and milk production, the current procedures, which last around 21 days, allow for the generation of milk with normal solids content.

In 98 cows utilized in the study by Mellado *et al.* (2006) and in 78% of the cows used in the study by Ramgattie *et al.* [26], respectively, the response to the stated lactation induction strategy was 100%. According to milk production, a volume of 77.2% from the previous lactation and 78% of dairy production from cows that gave birth normally were described [33]. There is a discrepancy in the data regarding the reproductive efficiency of the animals, with Freitas *et al.* [33] reporting that lactation induction protocols were used to induce lactation in 41.4% of pregnant Holstein cows, while Mellado *et al.* (2006) found no difference in the proportion of pregnancies between induced and non-induced dairy cows (71% of pregnancies) in Mexico.

Table 10: Biochemical profile and body condition score from control cows and induced cows at 21 days in milk

Variables	Control cows	Induced cows
Total Protein (g/dL)	7.73±0.18	7.68±0.18
Albumin (g/dL)	2.92±0.12	3.23±0.11
Globulins (g/dL)	4.92±0.30	4.41±0.24
Urea (mmol/L)	4.01±0.31	4.89±0.31
Creatinine (mg/dL)	0.97±0.06	1.30±0.06
BHBA (mmol/L)	0.50±0.03	0.43±0.04
Triglycerides (mg/dL)	10.23±1.51	14.33±1.52
Cholesterol (mg/dL)	97.17±8.57	78.18±7.56
GGT (U/L)	15.11±2.97	22.11±2.98
AST (U/L)	66.11±6.55	71.22±6.56
BCS (points)	3.04±0.24	3.50±0.20

Economics

One can fairly compare streams of money over time by using net present value analysis, which takes into account the value of money over time. When induced cows were compared to peer first-lactation cows, the NPV were considerably greater for the induced cows. Even though the amount of milk produced by induced cows and peer first-lactation cows was comparable, keeping existing herd animals was more profitable. The main element that affected the profitability of replacement heifers was animal cost. A heifer costs $1200 to acquire, whether through purchase or rearing, which is a significant investment that must be recovered through subsequent milk sales.

NPV advantage of induced lactation grew as heifer replacement cost increased, as seen by the analysis with 20% higher and lower replacement costs. In addition, the benefit of forced lactation rises to $819 per cow per year as the difference between the cull price and cow value (now $700) increases to $1000(Bach, 2023). The enhanced NPV of induced animals in comparison to peer first-lactation cows shows that induced lactation appears even more beneficial when milk prices are lower. Additionally, because the induced cows had larger percentages of milk protein and fat than their peer first-lactation cows, their milk was more valuable.

It more profitable to induce lactation in non-breeder cows compared to purchasing replacement heifers as for induced cows net present value (NPV) was $520 US greater than that for replacement heifers [11]. However, no economic benefit in using artificial induction was reported by Macrina et al., [102]. Net present value for an induced cow (1966) was significantly greater than that for a first-lactation cow [19]. Obtaining a calf from an infertile animal is an additional profit (Table 11).

Table 11: Net Present Value (NPV) Values for Induced and Culled Animals

Scenario	NPV (TT$)	References
Lactation Induced Cow	7397.70	(Ramgattie *et al.,* 2014)
Lactation Induced Heifer	5483.14	
Replacement Cow (Pregnant)	6302.24	
Replacement Cow (Not Pregnant)	3430.40	

Dairy farmers may save a lot of money if they were allowed to keep valuable cows that don't conceive but are still in good health. If each year, 24 percent of animals are put to death, with 26.7% of those being killed for reproductive purposes [21], then 6.4% of the entire herd is put to death for reproductive purposes. A 500-cow dairy would induce lactation in 32 cows per year as opposed to culling them using this involuntary cull rate of 6.4%. This results in an NPV advantage of $16,640 per year at a $520 yearly NPV advantage per cow.

Our profitability projections are cautious because our model did not account for expenditures associated with insemination and health. The peer first-lactation cows' insemination expenses would have been higher since more services were needed per pregnancy than with the induced cows. Additionally, the induced cows did not have any of the expensive post-calving conditions such milk fever, ketosis, retained placenta, or displaced abomasum.

Additionally, the use of bST in induced cows seems to be advantageous. Our projection of $261 per cow per year is based on the cows' response to bST during the course of the trial's 70-day run. One can anticipate that the milk yield increases brought on by bST for the course of lactation will resemble those observed in the final cycle of our treatment period because the maximal production response to bST comes after several injection cycles [11]. Compared to untreated controls, bST-treated cows produced 21.9% more milk over the course of the previous 14 days. If this number had been used to calculate the milk output of the 12-month control cows, the profitability of bST use would have increased even further.

This additional milk production could represent the economic benefit of the use of VEL-rbST for the farmer. The additional economic income due to the effect of the application of the rbST formulations is presented in (Table 11) In primiparous cows, the application of ZSO-rbST and VEL-rbST had an additional increase of US $0.13 and US $0.58 per day, respectively, while in multiparous cows, this increase was US $0.05 and US $0.66 per day for ZSO-rbST and VEL-rbST, respectively. The calculations consider the average additional milk production per rbST (kg/cow/day), cost of rbST ($/cow/day), and price of milk ($/kg).

Similarly, Posada et al. [73] performed in Colombia a micro economic analysis in order to establish a benefit/cost ratio, reporting that the rbST-treated group exhibited the best ratio. As indicated also by Tauer [103] over the 20 years that this technology has been used in the USA, annual decreases in the cost of producing milk demonstrate that rbST is a cost-reducing technology. Mean net present value (NPV) for induced cows ($1966) were significantly higher than that for peer first-lactation cows ($1446) [19]. This is an annual NPV advantage of $520 per cow induced into lactation. If actual milk price had been 20% higher, the NPV advantage for induced cows would decrease to $489. With a milk price 20% lower, the NPV advantage increased to $553. As expected, NPV advantage for the induced cows increased with higher replacement cost ($639) and decreased with lower replacement cost ($400; Table 12). In all cases, NPV was greater for the induced cows than for the peer first-lactation cows [19].

Table 12: Net present value, in dollars, of a 12-mo stream of net incomes for cows induced into lactation and peer first-lactation cows

Net present value	Induced cows	Peer first-lactation cows
Actual	1966	1446
Milk prices 20% higher	2422	1933
Milk prices 20% lower	1509	956
Replacement cost 20% higher	2058	1419
Replacement cost 20% lower	1873	1473

Sources: Magliaro, *et al.,* 2004.

Data used in net present value analysis included milk price ($0.297/kg), fat premium or discount per 0.1% over or under 3.5% ($0.0033/kg), protein premium or discount per 0.1% over or under 3.2% ($0.0055/kg), milk hauling charge ($0.013/kg), induction treatment ($10.58/cow, materials only), bST treatment ($6.07/injection), daily feed ($3.93/animal), and values of calf ($100), cull animal ($500), and milking animal ($1200). A discount factor of 6% was used. These values were chosen based upon current market rates in Pennsylvania at the time of the study or were calculated based on cost of materials and labor. A projected comparison of bST profitability in induced cows estimated that the annual NPV advantage for treating induced cows with bST would average $261/cow [19].

The current review examines the economic worth of cows that have been artificially instigated to become lactating. It also offers statistics about induced cows found in other works pertaining to experimentally instigated lactation cows and beyond. Farmers can earn from subsequent lactation in addition to the cows' forced lactation. Actually, the fact that induced cows gave birth to calves following the induced lactation demonstrates that induced lactation also provides a method to stop the loss of important genes from the herd for cows with high genetic merit.

SUMMARY AND RECOMMENDATION

For high-yield cows with limited fertility, induced lactation may be a viable alternative to natural lactation. It only makes sense to use it when the animal has been rendered infertile because it helps to decrease culling losses and increase earnings. In artificially inducing lactation in cows, prolactin supplementation enhances reproductive performance and milk composition. This supplement exhibits hormone interactions that work in concert, possibly enhancing milk production. Artificial induction of non-pregnant cows could decrease culling and boost revenue. The milk generated with this method is comparable to milk produced following a typical calving and is suitable for human consumption after a week. Heifers can also be used for economic gain by hormonally inducing lactation. More milk is produced by cows that have been given estrogen and progesterone to stimulate lactation than by untreated cows.

This technique might provide dairy farmers a management choice to boost profitability if it receives FDA approval. Along with estrogen and progesterone, prolactin is a hormone that is crucial for lactogenesis. Cattle's blood prolactin levels rise prior to birth, and this increase is required for full lactogenesis. Although bromocriptine can decrease milk production, prolactin injections can increase it. Two rbST formulations have different effects on milk production in primiparous and multiparous cows. The farmer's financial situation was enhanced by the fact that VEL-rbST produced more milk than ZOS-rbST, according to the review. Under the two formulations, there were no obvious differences in the cows' physical state. Overall, VEL-rbST might be a way to boost the dairy industry's profitability in hot climates. The pituitary gland is stimulated by regular milking and udder massage to release hormones that aid in the development of the mammary gland, milk synthesis, and milk secretion. Animals that have been fed adequately, scored well on body condition exams, and have healthy udders and teats respond to the treatment more favorably. In general, cows and buffaloes with artificially induced lactation yield 60 to 70 percent less milk than usual. In contrast to ZOS-rbST, VEL-rbST encouraged greater milk production, which boosted farmer income and offered a potential solution for increasing the profitability of the dairy industry in tropical climates. In fact, the fact that induced cows produced calves after the induced lactation shows that induced lactation also offers a way to prevent the loss of crucial genes from the herd for cows with high genetic merit. For cows with low fertility but good yields, induced lactation may be an alternative. Hormones can be used to artificially induce lactation in place of natural lactation, reducing culling losses in the herd and improving profits. Both the rate of involuntary culling and genetic losses are decreased by artificial induction. Induction of lactation is the most suitable procedure employed under tropical conditions to save such genetically superior bovines.

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