Prostaglandin based estrus synchronization in cattle: A review
Amare Bihon and Ayalew Assefa

Abstract: Reproductive cyclicity provides cattle with repeated opportunities to become pregnant. Understanding the physiology and endocrinology of the estrus cycle gives a great opportunity for reproductive management and control of the estrus cycle. To manage and control the cycle, there are lots of assisted reproductive technologies, of them estrus synchronization with prostaglandins (PGF2α) is the one. PGF2α is known to have the ability to regress the corpus luteum (CL). The success of the synchronization program is limited by numerous intrinsic and extrinsic factors like proper levels of nutrition, body condition, health, good estrus detection technique, semen quality, proper time of insemination, and efficiency of AI technicians. However, inadequacy in any of these areas can spell disaster for an estrus synchronization program. The choice of a protocol which fits the specific situation under consideration is the base for the success of any prostaglandin-based estrus synchronization programs. As a conclusion, the choice of technically right and practically feasible protocol is essential for a successful breeding program.

Subjects: Biology; Biotechnology; Agriculture

Keywords: cattle; estrus cycle; prostaglandin; synchronization

1. Introduction
According to the reports of Ahlawat et al., (2015), Roelofs and Kooij (2015), and Gokhan et al. (2010), animal breeding and reproduction are at the top of animal production pyramid indicating, good reproduction is a key for successful dairy operation with the highest fertility. For addressing food security and livelihood improvement in developing countries, strategic dairy sector...
development is the key. For successful dairy operation, selection of the most promising breeds and cross-breeding are considered as a practical solution (Tadesse, 2010).

Estrus synchronization and AI programs are sides of a coin (Lijalem et al., 2015). Considering physiology and endocrinology of the estrus cycle gives an enormous chance for reproductive management and control of the estrus cycle (Senger, 2005; Perry, 2004). For doing this, estrus synchronization is one of the realistic solutions (Islam, 2011; Ahlawat et al., 2015). It requires adequate nutrition, good body condition, high-quality semen, health, efficient estrus detection technique, appropriate postpartum period, and efficient AIT (artificial insemination technician). However, inadequacy in any of these areas can predict failure for an estrus synchronization program (Smith, et al., 2012; Cushman et al., 2007; Gizaw et al., 2016; Gupta et al., 2008; Lamb, 2013; Sprott & Carpenter, 2007; Troxel, 2012).

According to Maqhashu et al. (2016) report, assisted reproductive technologies (ARTs) are prejudiced by a lot of inherent and extrinsic factors. Especially, technologies using hormonal interventions have been implemented to increase the likelihood of estrus detection, insemination, and to increase pregnancy rates in different management systems. Estrus synchronization works either by controlling follicular development, promoting ovulation in anestrus cattle, regressing the corpus luteum in cyclic animals or synchronizing estrus and (or) ovulation (Lucy et al., 2004). Flourishing synchronization program results in higher synchronization, conception, and pregnancy rates (Lamb, 2013). However, availability, regularity, and competence of AI service are beneath the expectation of farmers (Gizaw et al., 2016) because they estimate the technology based exclusively on the production of the calf. If all the requirements are fulfilled, first service conception rates may approach 75%. However, the most accurate estimate is 50 to 55% (Gizaw et al., 2016; Troxel, 2012).

The program improves reproduction efficiency by reducing the calving interval, schedule calving season and milk availability, production of uniform calf crops, increasing calf weaning weights, and efficient use of artificial insemination technique (Galina & Orihuela, 2007; Islam, 2011; Girmay et al., 2015).

PGF2α is the effective leutolytic agent used for estrus synchronization in ruminants. Synchronization of estrus by it and its potent analog is the drug of choice in the reproductive management of bovine species (Ahlawat et al., 2015). Nowadays, a variety of protocols for estrus synchronization in cattle is designed and implemented (Gizaw et al., 2016). However, the selection of technically right and practically feasible protocol is the base for success (Gizaw et al., 2016; Gupta et al., 2008). Therefore, the objective of this review paper is to summarize the role of prostaglandins in cycle control and factors affecting its success.

2. Follicular dynamics in cattle
Non-growing (primordial follicles) and growing (primary, secondary and tertiary) population of follicles are found in the ovary undergoing either development or degeneration as a wave-like pattern. It occurs throughout the reproductive life by the processes of recruitment, selection, dominance, and atresia by entering from the non-growth phase to a growing population (Kanitz et al., 2001; Oliveira et al., 2011; Senger, 2005; Wilhelm, 2003). According to Arthur (2001), Senger (2005), and Wilhelm (2003)’s report, follicular recruitment occurs every 8–10 days while the secretion of inhibin by the dominant follicle (DF) plays an important role on it (Zacarias et al., 2015). Luteal regression (progesterone withdrawal) is followed by rapid maturation of the DF to increase the level of estradiol, which makes LH surge to ovulate it (M. C. Lucy et al., 2004). Almost 95% of the estrus cycle consists of two or three follicular waves in bovine species (M. C. Lucy et al., 2004; Chasomba et al., 2014; Kanitz et al., 2001; Viana et al., 2000).

3. Estrus cycle of cattle
The estrus cycle is a vibrant process ranging from 18 to 24 days with an average of 21 days in cattle. Cycle length out of the range is considered abnormal (Senger, 2005). According to reports of
Viana et al. (2000) and Kanitz et al. (2001), the length of the cycle is similar in cycles with different follicular waves. It consists of follicular phase (preestrus, estrus) and luteal phase (metestrus and diestrus) (Perry, 2004, Fact sheet IRM-2 and Birhanu et al., 2015). Estrogen and progesterone are the dominant hormones on the follicular and luteal phase, respectively. The period when the animal is devoid of a cycle is the anestrus stage, which may be physiological (pregnancy, failure of estrus detection, a season of the year, lactation) or pathological condition (Kumar, 2014; Senger, 2005).

4. Prostaglandin (PGF2®) and its role in cycle control
Prostaglandin is produced naturally in different parts of the body especially in the ovary to cause functional or structural regression of the corpus luteum. Regression of the corpus luteum results in the removal of progesterone negative feedback control and development of follicles for the next wave. Luteolysis is characterized by a decrease in the secretion of progesterone (P4), luteal size, and blood flow in cattle but increase in E2 (estradiol) concentration (Araujo et al., 2009; Galina & Orihuela, 2007; Ginther et al., 2011, 2007; Sprott & Carpenter, 2007; Stocco et al., 2007).

After it is identified as the luteolytic agent, its commercialization follows with natural and synthetic forms to shorten the luteal phase, which makes it economically feasible for synchronizing estrus (Cordova-Izquierdo et al., 2009; Diaz et al., 2005; Ginther et al., 2010; Paul et al., 2015, 2015; Sprott & Carpenter, 2007) and M. C. Lucy et al. (2004). It will operate in single and double injection systems alone or combination with other hormones. The report of Ahlawat et al., (2015) stated that double injection has a better response rate than single injections.

According to Sprott and Carpenter (2007) and Paul et al. (2015)'s report, in cyclic females estrus occurs within 3 to 8 days after they are given intramuscular injections of PGF2α (Lutalyse®) or one of its analogs (Prostamate®, Estramate®, estroPLAN®, In-Synch®) depending on the day of injection and the presence of dominant follicles. It only acts during the luteal phase of the cycle (Sprott & Carpenter, 2007).

5. Success rates of prostaglandin-based synchronization programs
Numbers of estrus synchronization programs are available in cattle using PGF2α hormones alone or in combination with other hormones like progesterone, estrogen, and Gonadotrophin-Releasing hormone (GnRH) (Islam, 2011; Sprott & Carpenter, 2007; Troxel, 2012) (Table 1).

6. Factors affecting the success of synchronization program
The success of the dairy operation is influenced by biological, environmental, and management factors. Due to these factors, it is difficult to achieve “one calves per one year principle” while it is considered as an economically feasible and optimal success for dairy operation (Anderson et al., 1991; Million et al., 2011; Murugavel et al., 2010; Senger, 2005).

6.1. Heat detection and insemination time
According to the reports of Gupta et al. (2008), Cirit et al. (2008), Sveberg et al. (2011), Roelofs and Kooij (2015), and Paul et al. (2015) heat detection is a major limiting factor and the base for success. Failure of estrus detection results in infertility in cattle (Gatius et al., 2005; Cirit et al., 2008; Girmay et al., 2015, Fact Sheet IRM-2; Paul et al., 2015). Generally strict follow up, the use of heat-detector devices and technologies helps to increase detection ability to have successful breeding (Cirit et al., 2008; Jemal et al., 2016). Detecting estrus many times a day as much as possible is better than detecting estrus once a day (Girmay et al., 2015; Troxel, 2012). For the last seven decades, the standard for the time of insemination recognized as 12 h after onset of estrus (Dorseya et al., 2011) is supported by the findings of Legesse, (2016) and Roelofs et al. (2006) stating the higher degree of conception achieved at 10–15 h of insemination after the onset of estrus.
Table 1. Summary of different PG-based synchronization programs

| Authors              | Type of Rx              | Estrus response (%) | Conception/ pregnancy rate (%) | Calving rate (%) |
|----------------------|-------------------------|---------------------|--------------------------------|-----------------|
| Venkata Ramana et al. (2013) | Double PG               | 82                  | 67 ± 0.26                      | -               |
| Gupta et al., 2008   | Double PG+FTAI          | -                   | 55                             | -               |
| Weldyesus et al. (2016) | Single-shot PG          | 100                 | 61                             | -               |
| Girmay et al. (2015) | One-shot PG             | 91.3                | 32.17                          | -               |
| Zeuh et al., 2014    | One-shot PG             | 76.47               | 29.41                          | -               |
| Ahlawat et al., (2015) | 1<sup>st</sup> PG    | 30                  | 43.05                          | -               |
|                      | 2<sup>nd</sup> PG      | 57                  | 49                             | -               |
| Legesse, 2016        | One-shot PG             | 87.2                | 42.2                           | -               |
| Gugssa (2015)        | Singe+ double PG        | 87.2                | 62.7                           | -               |
|                      | Single-shot PG          | 84.2                | 59.6                           | -               |
|                      | Double PG+ heat detect  | -                   | 68.5                           | -               |
|                      | doublePG+ FTAI          | -                   | 48.9                           | -               |
| Small et al. (2001)  | Double PG +FTAI        | 75.9                | -                              | -               |
|                      | Ovysynch +FTAI         | 51.4                | -                              | -               |
|                      | Modified ovysynch+FTAI-| 71.3                | -                              | -               |
| Murugavel et al. (2010) | One shot PG         | 55.56               | 33.33                          | -               |
| Tegegne et al., 2012 | One shot PG awassa-dela milk shed | 97.7 | 57.7 | - |
|                      | One shot PG adigrat-mekie milk shed | 100 | 61.7 | - |
| Bainesagn, 2015      | Single shot PG         | 72.32               | 57.44                          | -               |
|                      | Single +double PG      | 83.85               | 52.29                          | -               |
| Tewodros et al., 2015 | Single PG              | 98.92               | 26.88                          | 26.9            |
|                      | Natural mating         | -                   | 32.07                          | 32              |
| Adebabay et al., 2013 | One shot PG            | 89.3%               | 13.7%                          | -               |

6.2. Body condition and nutrition

Body condition score (BCS) of an animal is a means to assess physiological states, energy reserves, and rebreeding potential of animals (Ciptadi et al., 2012). Poor nutrition is the main cause of infertility in cattle reared in tropical (Bó et al., 2003; Rekwot et al., 2004) and other regions (Baru et al., 2003; Berry, 2003; Ciptadi et al., 2012; Schroeder & Staufenbiel, 2006). The reports of Cutaia et al. (2003), Johnson and Stevenson (2003), Jemal et al. (2016), Girmay et al. (2015), Bainesagn (2015), Spitzer et al. (2007), Kouamo and Sawadogo (2012), and Maqhashu et al. (2016) state synchronization implemented with a poor body conditioned animals results in a low level of heat response and pregnancy rates.

6.3. Parity

The results of different studies clearly indicate the effect of parity in different protocols of the synchronization program. However, the effect should depend on the health status and management of dairy animals (Herlihy et al., 2011; Gizaw et al., 2016; Mwaanga et al., 2012; Girmay et al., 2015; Bainesagn, 2015; Malik et al., 2012).
6.4. Insemination service and insemination technicians

Insemination service is delivered as a daily round of inseminators, static point insemination and cell phone-based systems (Tadesse, 2010 and Gebremichael, 2015). The major problems of insemination in-tropics include technical limitation, lack of transport facility, poor quality of semen, timely unavailability of semen, poor heat detection, lack of incentives, unavailability of the service off- working hours, high cost of service, and low efficiency and shortage of AI technicians (Tegegne et al., 2012, Birhanemeskel, 2014; Gizaw et al., 2016; Gizaw & Dima, 2016, Legesse, 2016). For example, the efficiency of AI service in Ethiopia is very low with the conception rate to the first service being 27.1% according to the findings of Desalegn et al. (2009).

There is great variation in terms of the skill of technicians in detecting the presence of functional corpus luteum for hormone administration and effective AI service (Sprott & Carpenter, 2007; Gizaw et al., 2016; Troxel (2012). For example, according to Gugssa (2015)’s report from Ethiopia, on average one technician misclassified 4.6 cows out of 10 cows presented for corpus luteum detection. In general, the use of experienced technicians can help to ensure conception in females that respond to treatment (Gizaw et al., 2016; Sprott & Carpenter, 2007; Troxel, 2012).

6.5. Semen quality

According to the recommendation of IAEA (International Atomic Energy) and FAO (food and agricultural organization) (IAEA [International Atomic Energy Agency] and FAO [Food and Agriculture Organization of the United Nations], 2005), acceptable semen should have 40% or more actively forward-moving spermatozoa after freezing and thawing while semen motility and viability is influenced by AI centers (collection up to packaging), storage conditions, level of contamination, thawing procedure and temperature, reproductive health of bulls, and genetic and morphological differences among semen products (Adebabay et al., 2013; Birhanemeskel, 2014; Bainesaghn, 2015; Girmay et al., 2015; Mulugeta and Belayeneh, 2013 and Legesse, 2016).

7. Conclusion

Understanding the estrus cycle is the base for the manipulation of reproduction in cattle. Prostaglandin-based estrus synchronization programs are effective for cycle control in the responsive phase of the cycle. If correctly implemented by considering all the factors, prostaglandin-based synchronization program is successful.

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