Chapter

Bibliographic Review of the Application of Ovulation Synchronization Protocol Based on Gonadotropin-Releasing Hormone (GnRH) and Insulin to Increase the Conception Rate in Crossbred Holstein Cows

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Abstract

The review work is based on analyzing and recording the effects of the application of ovulation synchronization protocols based on gonadotropin-releasing hormone (GnRH) and insulin for the increase of the pregnancy rate in crossbred Holstein cows in research published between 2013 and 2017. The study was conducted through the integrated search of relevant authors' research using key criteria of both inclusion and exclusion, with results from 244 articles analyzed, where 118 analyzed the interaction of energy balance and ovulation of dairy cows. Fifty-three articles relate the effective ovulation synchronization protocol for the luteal process and 73 articles analyze the effect of insulin in the luteal process; and finally 18 articles are important to address the problem; insulin can be altered as a metabolic hormone by the increase of fat components of the feed ration consumed by cows, thus influencing ovarian function; ovulation synchronization is necessary, which can be based on GnRH and insulin.

Keywords: ovulation, insulin, hormone, GnRH, fertility

1. Introduction

In the present work, the results of the bibliographic study of the published scientific articles are detailed in Journals such as *Boletim Industrial Animal*; *American Dairy Science Association*; *Veterinary (Montevideo)*; *Animal Health Magazine*; *Cuban Journal of Agricultural Science*; *SMVU MAGAZINE*; *Scientific Information System Redalyc*; *Theriogenology*; *Reproduction, Fertility and Development*; *BioMed Research International*; and *Biotechnology Advances* in the last 5 years.

The analysis of the information documents is made based on the references of published works, understanding that they represent the scientific information

used in the preparation of various investigations, both to justify and to compare results obtained. The reasons why the authors choose some references and not others are related to several factors. Many of the investigations carried out in the field of the application of the ovulation synchronization protocol, gonadotropin release (GnRH), and insulin use to increase the pregnancy rate of dairy cattle tend to use literature in English in their bibliographical references, with the convinced that this gives more prestige to work. On the other hand, bibliography also selects works published in journals recognized by the main databases, in order to support research that is recognized by the journals that have published them, which obtain, in turn, the databases.

It should be mentioned that follicular growth including the final maturation of the oocyte takes between 8 and 12 weeks in cattle [5]. The metabolites and hormones such as insulin preserves change in concentration in the serum according to the metabolic condition; similarly there is a change following the same pattern in the follicular fluid, although the concentrations may differ [2, 3]. This implies that the oocyte may be exposed to metabolic changes during development and its final maturation.

The majority of high production dairy cows experience a negative energy balance (NEB) in early lactation. The postpartum insemination often occurs around 60 days postpartum so the presumed oocyte for fertilization begins to grow during the dry period before parturition [3, 5].

High and low levels of insulin influence fertility and early embryonic development. The beneficial effects of the different levels of insulin act if the individual is in a state of metabolic homeostasis where the system manages to adapt in response to changes in the energy supply. More studies are needed to get a more complete picture of how insulin concentrations during different reproductive periods correlate with fertility [11].

In addition to increasing the concentration of cholesterol, fat supplementation has increased progesterone plasma concentrations [7, 8, 12, 19, 20]. This has been due to the hypothesis being related to the increase in plasma concentrations of cholesterol, the precursor for steroid synthesis [22].

Intrinsic mechanisms involved are not known in decreased oocyte quality caused by excess energy; some authors have attributed negative excess insulin results because there are changes in the concentrations of other hormones they have studied as IGF-1 and leptin [1]. However, leptin and local growth factors are involved in mechanisms through which diet can affect the quality of oocytes [25]. In addition, adequate concentrations of IGF-I are important for follicular growth and oocyte maturation [10], because excessively bioavailable IGF-I reduces oocyte competition [2].

The objective of this study is to analyze and review the effects of the application of ovulation synchronization protocols based on gonadotropin-releasing hormone (GnRH) and insulin for the increase of the pregnancy rate in crossbred Holstein cows.

2. Materials and methods

The search strategy for the identification of the studies has been divided into three phases:

Phase I. Detailed search in the scientific databases based on the search questions, search strategy, and information sources being the magazines, such as *Boletim de Indústria Animal*; *American Dairy Science Association*; *Veterinary (Montevideo)*; *Animal Health Magazine*; *Cuban Journal of Agricultural Science*; *SMVU MAGAZINE*;

Scientific Information System Redalyc; *Theriogenology*; *Reproduction, Fertility and Development*; *BioMed Research International*; and *Advances in Bioscience and Biotechnology*, to the rest in the search engine, search criteria, and inclusion and exclusion criteria, in the content evaluation criteria (**Table 1**).

Appearance	Explanation
Search questions	• How does the deficiency of luteinizing hormone affect the process of luteolysis? • What ovulation synchronization protocol is the most effective for the luteolysis process to be accomplished and to increase the conception rate in crossbred Holstein cows? • Is the ovulation synchronization protocol including insulin effective for the luteolysis process to be met and for the conception rate to increase?
Search strategy	• Area: Reproduction of dairy cattle • Define the most effective ovulation synchronization protocol including insulin so that the luteolysis process is completed and increases the conception rate
Information sources	• Journals indexed between 2013 and 2017
Search engine	• Google Scholar
Search criteria	• Effect of increase in circulating insulin concentrations • Effects of a diet on oocyte • Effect of insulin concentrations postpartum period • Increase ovulatory response • Ovarian response in Holstein cows • Energy and its effect on cholesterol • Reproductive state of Holstein cattle • Formulations of estradiol and progesterone • Effect of a single injection of progesterone
Inclusion criteria	• Insulin • Effect of preovulatory cholesterol, hormonal profile • Deficiency • Ovulation • Estradiol • Progesterone • Dairy cows • Fertility
Exclusion criteria	• Food, meat, goat, canine, lamb
Criteria evaluation of the contents	• The synchronization of ovulation is an excellent technique to increase reproductive efficiency in crossbred Holstein cows, which favors directly the conception rate, the multiple gonadotropin-releasing hormones shorten the time of the luteal phase in order to increase the fertility of animals, and through insulin induce ovulation, interacting the negative energy balance in this process
Analysis of the information	• Applied method that is more efficient for AI, in Holstein cows • Gynecological evaluation periodically to select the best ovulation synchronization protocol and in the same way the most profitable protocol

Table 1.
Search method.

N°	Article name	Authors	Year
1	Effects of supplementation with protected polyunsaturated fatty acids on productive and hormonal parameters of embryo recipient heifers	Juan Camilo Angel Cardona, Harold Ospina Patino, Monica Marcela Ramirez Hernandez, Carolina Heller Pereira*, Kendall Swanson	2016
2	Effects of a high-energy diet on oocyte quality and in vitro embryo production in *Bos indicus* and *Bos taurus* cows	JNS Sales, LT Iguma, RITP Batista, CCR Quintão, MAS Gama, C. Freitas, MM Pereira, LSA Camargo, JHM Viana, JC Souza, PS Baruselli	2015
3	Dry period plane of energy: effects on glucose tolerance in transition dairy cows	S. Mann, FA Leal Yepes, M. Duplessis, JJ Wakshlag, TR Overton BP Cummings, and DV Nydam	2016
4	Manipulation of progesterone to increase ovulatory response	PD Carvalho, MC Wiltbank, PM Fricke	2015
5	Ovarian response and hormone levels in hello cows in different reproductive stages treated with Ovsynch and two progesterone formulations	Cavestany D, Martínez-Barbitta M, Alonzo A, López R, Pilón A, García ME, Segredo A, Sosa N	2016
6	Energy supplementation and its effect on cholesterol levels and preovulatory hormonal profile in cows/energy supplementation and its effect on the level of cholesterol and the preovulatory hormonal profile in cows	Monica Andrea, Moyano Bautista, Carlos Eduardo Rodríguez	2014
7	Metabolic and reproductive state of Holstein cattle in the Carchi region, Ecuador	LR Balarezo, JR García-Díaz, MA Hernández-Barreto, and R. García López	2016
8	Comparison of different estradiol and progesterone formulations	Martínez-Barbitta Ma, González-Guasque Wb, Martínez-Piña Mb, Cavestany Dc	2015
9	Effect of a single injection of progesterone, 5 days	Carlos I. Roque-Velázquez, Hugo H. Montaldo-Valdenegro, Carlos G. Gutiérrez-Aguilar, Joel Hernández-Cerón	2016
10	Relationship between circulating progesterone at timed-AI and fertility in dairy cows	MG Colazo, I. Lopez Helguera, A. Behrouzi, DJ Ambrose, RJ Mapletoft	2017
11	Association between polymorphisms in somatotropic axis genes and fertility of Holstein dairy cows	Lucas Teixeira Hax, Augusto Schneider, Carolina Bespalhok Jacometo, Patrícia M. Attei, Thaís Casarin Da Silva, Géssica Farina, Marcio Nunes Belt	2016
12	Epidemiological evidence for metabolic programming	G. Opsomera B, M. Van Eetveldea, M. Kamala, and A. Van Soom	2017
13	Hypothyroidism reduces the size of ovarian follicles and	J. Rodríguez-Castelán, M. Méndez-Tepepa, Y. Carrillo-Portillo, A. Anaya-Hernández	2017
14	Effects of supplemental dietary energy source	Xueyan Lin, Guimei Liu, Zhengyan Yin, Yun Wang, Qiuling Hou, Kerong Shi, Zhonghua Wang	2017
15	Elevation of blood β-hydroxybutyrate concentration effects	M. Zarrin, L. Grossen-Rösti, RM Bruckmaier, and JJ Gross	2016
16	Single-dose infusion of sodium butyrate, but not lactose, increases plasma β-hydroxybutyrate and insulin in lactating dairy cows	KJ Herrick, AR Hippen	2016
17	The effect of subclinical ketosis on activity at estrus	Andrew J. Rutherford, Georgios Oikonomou and Robert F. Smith	2015
18	Increasing estrus expression in the lactating dairy cow	JA Sauls, BE Voelz, SL Hill, LGD Mendonça, and JS Stevenson	2016

Table 2.
Most important scientific articles.

Phase II. Analysis of the bibliographic citations of the articles selected in the first phase, which are 18 and have been considered of greater importance for the approach of the problem, and are in the range of 5 years for the investigation (2013–2017), same which are reported in **Table 2**.

Phase III. Analysis of the scientific documents published in the journals mentioned in Phase I analyzed their bibliographic citations in phase II.

The search criteria that determine the selection of articles have the words of inclusion and exclusion; similarly, the specific interval of time was selected according to the order of relevance, including patents and citations (**Table 3**).

- Articles on experimental, quasi-experimental studies and studies related to the problem where the effect achieved by applying synchronization protocols based on gonadotropin-releasing hormone (GnRH) and insulin to increase the rate pregnancy in crossbred Holstein cows.

- Studies in which the validity and usefulness of the data are still valid today were analyzed from the 18 scientific articles mentioned in **Table 2**.

Search	Number of results	Specific time interval
Effect of increase in circulating insulin concentrations during the early postpartum period on reproductive function in dairy cow, insulin, reproductive or cattle	24	2015–2017
Effects of a diet on oocyte quality in *Bos indicus* and *Bos taurus* cows, high, or energy "in vitro embryo production"	78	2015–2017
Effect of insulin concentrations postpartum period on reproductive in dairy cow	5	Since 2016
Increase in ovulatory response to the first GnRH treatment manipulation, progesterone, or protocol "first timed artificial insemination," breed	12	Since 2015
Ovarian response in Holstein cows in "different reproductive stages"	4	Since 2015
Energy and its effect on cholesterol level cows supplementation cows energy affect effect preovulatory "hormonal profile "cholesterol-breed	7	Since 2014
Reproductive state of Holstein cattle metabolic energy state deficiency profile, metabolic or profile or bovine indicators, "Holstein cattle," breed	18	Since 2016
Comparison of different formulations of estradiol and progesterone cows or dairy or ovulation or estradiol or progesterone "synchronization of estrus" breed, tropical	3	Since 2015
Effect of a single injection of progesterone on the fertility of dairy cows, insemination fertility, effect on cows, dairy, ovulation, estradiol, progesterone, "after insemination," feed, meat	4	Any moment
Pregnancy rate in Holstein cow pregnancy or rate	11	2017
Treatment of polycystic ovary syndrome with insulin	3	2017
Sources of glucose in ruminants, gluconeogenesis, glucose, lipids, acids	15	2017
Relationship between insulin and present of estrus synchronization artificial protocol or insemination	19	Since 2016
Pregnancy rate percentage in Holstein cows, detection, estrus, insulin, progesterone, estradiol, hormone	41	2017

Table 3.
Search criteria.

3. Results and discussion

Between 2013 and 2017, a total of 597 references were cited in the Bibliography section of the original articles. The distribution by years (**Figure 1**) shows that the highest number of references occurred in 2016 (with 334 references, from 9 articles analyzed) and the lowest figures appear in the years 2013 and 2014 (with 0 and 18 references, from 0 and 1 original work, respectively).

3.1 Language

Eighty-three percent of the references come from documents in English and seventeen percent in Spanish (**Figure 2**). English predominates among the works published in scientific journals mentioned in Phase I.

3.2 Bibliographic analysis of scientific articles

Insulin is a key metabolic hormone that plays a crucial role in the regulation of energy homeostasis in the body [11].

There is a reduction of GHR expression in hepatic tissue in the postpartum dairy cows of high production due to the decrease in blood insulin concentration and negative energy balance (NEB) [20]. Accordingly, the reduction of GH binding in the liver decreases the synthesis of IGF-I. An increase in serum IGF-I is associated with an increase in estradiol production in ovulatory and early postpartum ovulation [4]. Early postpartum ovulation is associated with a shorter birth interval of delivery [21].

It is possible that cows in the semi-extensive system, characterized by lower milk production, are not subjected to a marked NEB. Consequently, these cows are not likely to have a reduction in postpartum GHR liver [20].

The strongly selected for milk yield dairy cows have specific endocrinological characteristics, as low levels of peripheral insulin and low peripheral insulin sensitivity, both contributing to safe guarding glucose milk production. The reverse side of this advanced selection is the high incidence of a wide range of metabolic diseases [15].

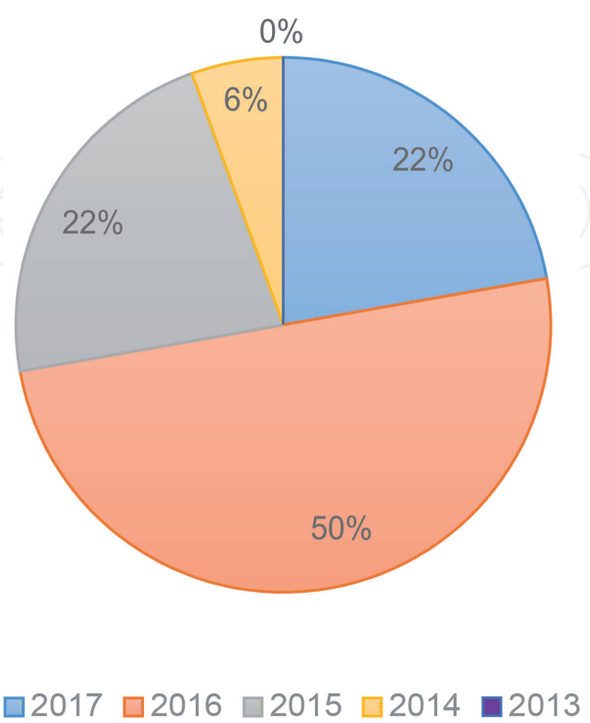

Figure 1.
Distribution of articles by year of publication.

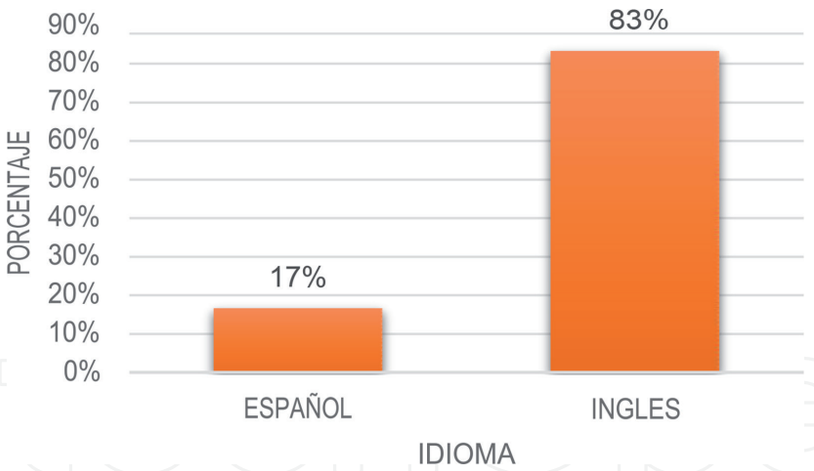

Figure 2.
Language of scientific articles.

Ovarian failure is related with inflammation as well as hypertrophy and visceral adipose tissue dysfunction (VAT). Although hypothyroidism has been associated with obesity, dyslipidemia, and inflammation in humans and animals, its influence on the characteristics of ovarian follicles in adulthood is poorly understood [18].

The source of supplemental dietary energy has variable effects on food intake and lactation performance and intermediary metabolism early lactation in a positive energy balance. The secretion of 5-hydroxytryptamine may be associated with the variable effects of the supplementary dietary energy source.

A higher basal insulin concentration before and after birth. These findings show that the effects of hyperketonemia about plasma glucose concentrations are similar before and after delivery but that endocrine hyperketonemia adaptation differs before and after delivery. B-assume hydroxybutyrate (BHB) is a key metabolic regulator in premature dairy cows and may affect glucose concentration for additional channels as gluconeogenesis and lipolysis altered [26].

Embryo-receiving heifers play an important role in the success or failure of embryo transfer. Some studies have shown positive effects of fatty acids on embryonic development [6, 12, 17, 24] and pregnancy rates [12, 13], which are also positively correlated with higher cholesterol [7, 23] and progesterone [7, 9, 12, 14, 16, 20].

4. Conclusions

The interest awakened from the effect achieved with the application of ovulation synchronization protocols based on the gonadotropin-releasing hormone (GnRH) and insulin to increase the pregnancy rate in crossbred Holstein cows is shown in the increase in publications in the last decade.

The most common strategy to reduce the degree of negative energy balance in early lactation is in reference to the concentration of energy in the diet since it increases the starch or fat components of the ration at the expense of the forage. These strategies alter metabolic hormones, particularly insulin, which can influence ovarian function.

Once the scientific articles have been analyzed applying the relevant methodology, it is concluded that insulin with GnRH may be a protocol that empirically provides benefits, but studies of better methodological quality are still needed to demonstrate the effects attributed to them.

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