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Pregnancy loss in the female bovine and strategies to improve efficiency in assisted reproductive

Pérdida de la preñez en la hembra bovina y estrategias para mejorar la eficiencia en los programas de reproducción asistida

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Abstract

In artificial insemination (AI) programs, repeated estrus and embryonic (EM) and fetal losses are important causes of low reproductive efficiency in hot climates. This literature review aims to show the causes and strategies to decrease pregnancy losses in cows. In cattle, the fertilization rate is high and occurs in approximately 75 to 90% of the inseminated females. Embryonic losses occur in more than 25% of the services and the highest proportion of them occurs between 15 to 17 days after service and six weeks after the beginning of pregnancy. Biotechnical procedures used to prevent repeat estrus and embryonic and fetal mortality include the use of exogenous hormones including progesterone, estrogens, growth hormone, human chorionic gonadotropin, hormone releasing factors and recombinant alpha interferon to enhance corpus luteum functions and inhibit the mechanism of luteolysis. Other procedures include the application of various biotechnical estrus synchronization and resynchronization procedures to improve the efficiency of AI services and correct low estrus detection efficiency. Feeding supplementation with unsaturated fat and antioxidants and management measures to reduce the impact of heat stress. These procedures can contribute to improve fertility of cattle in hot climates.

Keywords: repeat service; pregnancy losses; embryonic mortality.

Resumen

En los programas de inseminación artificial (IA), las repeticiones del celo y las perdidas embrionarias (ME) y fetales son causas importantes de la baja eficiencia reproductiva en los climas cálidos. Esta revisión bibliográfica tiene como objetivo mostrar las causas y estrategias para disminuir las pérdidas de la preñez en la vaca. En el ganado bovino, la tasa de fertilización es alta y ocurre aproximadamente entre el 75 al 90% de las hembras inseminadas. Las mermas embrionarias se producen en más del 25% de los servicios y de ellas la mayor proporción se produce, entre 15 a 17 días del servicio y las seis semanas de inicio de la preñez. Los procedimientos biotécnicas utilizados para prevenir las repeticiones del celo y la mortalidad embrionaria y fetal tales como: el uso de hormonas exógenos que incluyen la progesterona, los estrógenos, la hormona del crecimiento, la gonadotropina coriónica humana, los factores de liberación hormonal y el alfa interferón recombinante con el fin de potenciar las funciones del cuerpo lúteo e inhibir el mecanismo de la luteólisis. Otros procedimientos incluyen la aplicación de diversos procedimientos biotécnicas de sincronización y resincronización del celo para mejorar la eficiencia de los servicios de IA y corregir la baja eficiencia en la detección del celo. La suplementación alimentaría con grasa no saturada y sustancias antioxidantes y medidas de manejo para reducir el impacto del estrés del calor. Estos procedimientos pueden contribuir a mejorar la fertilidad del ganado bovino en climas cálidos.

Palabras clave: repetición del servicio; pérdidas de la preñez; mortalidad embrionaria.

Introduction

Cattle infertility is a multi-factor issue that may be related to the following factors: lower oocyte performance during maturation, embryonal fertilization and development, inefficient sperm transportation, problems during fertilization, changes in the composition of the uterine environment, implementation problems and the development of the embryo (Rizos et al., 2010).

One of the most studied infertility issues in bovines is pregnancy loss, since it is considered to be the main cause for the extension of the time periods between births, and which causes significant economic losses in the industry. In practice, these issues manifest themselves in: repeated estrus (non-fertilization) and embryonal or fetal deaths (Diskin et al., 2016; Wiltbank et al., 2016).

From the conception perspective, embryonic losses occur between the period after conception and the differentiation stage. Meanwhile, fetal losses occur from day 42 of gestation until the end of pregnancy (Zhang and Smith, 2015).

In the last two decades, there has been notable advances in the knowledge about the physio-pathological causes and mechanisms that produce repetitions in the artificial insemination services, and the embryonic and fetal losses (Hansen and Barron, 2011). This circumstance has allowed the development and the introduction of management strategies and biotechnical methods (Walhs et al., 2011), with the objective of improving cattle fertility in the artificial insemination programs (AI) and embryo transfer (ET).

In this context, the objectives of the literature review are as follows: to present the most prominent factors that cause estrus repetition and the embryonic and fetal losses in female bovines under artificial insemination programs and embryo transfer in grazing cattle, under tropical climate conditions; to show recent discoveries related to the process of pregnancy implementation and maintenance; the methods for diagnosing embryonic viability and the various management strategies and biotechnical procedures used to improve conception rate, and embryonic and fetal survival in female bovines under assisted reproduction programs.

Methodology

For the data analysis, PubMed, Scopus, Web of Science and Web Animal Science data bases were used as the main sources to obtain scientific papers related to the economic impact of pregnancy losses, the luteal phase and the classification, implementation and sustenance of gestation. The causes for embryonic and fetal mortality, pregnancy diagnosis and prediction of the viability of the treatment to improve fertility in artificial insemination and embryo transfer. In this context, 215 scientific articles related to the topic at hand, were reviewed.

Literature review

Economic impact and incidence of pregnancy loss after artificial insemination or embryo transfer in female cattle

The production chain of dairy and meat in bovines depends on its reproductive efficiency. Consequently, inadequate fertilization and pregnancy loss are inconveniences that cause great economic losses in different production structures and assisted reproduction programs. This phenomenon can be seen in three specific cases: non-fertilization, embryonic mortality and abortion. These are the causes for longer intervals between births, a decrease in dairy production and birth rates. They also shorten the lifetime of cows and negatively impact the implementation of genetic enhancement programs through artificial insemination and embryo transfer.

According to multiple studies, daily economic loss during the next 100 days post-partum amount between 3 to 5 USD per day. In the United States, the cost of pregnancy loss account for 1,4 billion every year. Meanwhile, in England the deficit amounts to 250 million pounds, and the cost per-capita ranges from 600 to 1000 USD.

It is evident that both global and per-capita numbers generated by pregnancy losses can vary and this is fundamentally dependent on: the management of cattle; the quantity and conditions of lactation; the gestation period in which pregnancy loss occurs; and the cost of artificial insemination and embryo transfer. Although these calculations cannot be easily extrapolated for the rest of the world, global costs are estimated to reach USD 280,000,000,000. These findings have served as the justification to conduct studies in this field for many decades. In this sense, Sartori et al. (2010) mentioned that before the use of AI, more than 80% of oocyte fertilization in cattle was successful. However, this number is slightly lower in warm climates because of caloric stress and the insufficient quality and efficiency of artificial insemination in some countries. In both contexts, the success rate could fall below 70%.

With regard to embryonic viability, recent studies point out that the results can vary widely, with estimates going from 20 to 91% (Yusuf et al., 2010). In reference to this, early embryonic mortality before day 25 after artificial insemination ranged from 4.5 to 43.7%. Meanwhile, late embryonic mortality between day 25 and day 42, and fetal mortality after day 50 ranged from 8.3 to 24.0% in lactating cows and from 1 to 10.2% in inseminated heifers. These percentages were even lower in female specimens raised for meat production. Pregnancy loss went from 4 to 10.8% in this last group.

Brief summary of the luteal phase and the classification, implementation and sustenance of pregnancy in female bovines

The luteal phase and pregnancy sustenance are two antagonistic physiological processes. In this sense, endometrium cells play an important role acting as highly-specialized complex endocrine tissue, made up by two types of cells: fibroblastic stromal (FSC) and glandular epithelial cells (GEC), both of which help regulate the estrous cycle in bovines through stimulus signaling and synthesis of prostaglandins. FS and GEC respond to various molecular, physiological and pathological stimuli to regulate PGF2 α and PGE2 production (Olivera, 2010).

These stimuli must activate molecular pathways in a coordinated manner to select the type of prostaglandin that is needed to be synthesized. In turn, in the glandular epithelial cells, basic production of PGF2 compared to PGE2 is 105 and 53 $pg \cdot mL^{-1}$, respectively, that is, PGF2 α is two times higher, and it shows that epithelial cells have higher luteal capabilities. On the other hand, FSC produced both prostaglandins. However, the proportion of PGE2 production was eight times higher than PGF2 α (2,6 $ng \cdot \mu g^{-1}$ vs 0,34 $ng \cdot \mu g^{-1}$), which suggests that these cells have higher autotrophic capabilities (Olivera, 2010).

Other circumstances related to the luteal phase are the many physiological events that go alongside said phase during an inflammatory process modulated by the hormones produced by the corpus luteum (CL) and the non-ovulatory ovarian follicle. In the first phase, the action plan by the progesterone and the estrogens (E2) segregated by the CL and the non-ovulatory ovarian follicle. The latter hormone (E2) is tasked with stimulating oxytocin (OXT) receptors in the endometrium. Afterwards, the OXT from the posterior pituitary as well as that which is segregated by the CL, activates the Protein kinase (PKc) enzymatic system, and in turn, the synthesis and secretion of the PGF2α from the endometrium.

Next, PGF2α activity inhibits the creation of LHr receptors in the CL cell membranes and the genic expression of the P450scc system, responsible for converting cholesterol into progesterone. Then, there is an increase in the local blood flow and the activity of innate immune system, characterized by an increase in macrophages numbers, lymphocytes and cytokines (Schütz et al., 2014), among which the interleukin-1β, the gamma interferon (IFN-Y), the Tumor Necrosis Factor (TNFα), and the Transforming Growth Factor (TGF), stood out. The collective activity of these components of the immune system produces degeneration of granulose cells and the theca, as well as the decrease of the synthesis and secretion of progesterone, and the apoptosis of the CL cells. This produces estrus repetition and early pregnancy loss in cows (Pedroso y Roller, 2021).

Pregnancy sustenance mechanism in female bovines

The follicular grow and development in pregnant cows are characterized by the increasing presence of small estrogen follicles and decreasing large active ones. Moreover, an active corpus luteum is required, an endocrine gland that grows from ovarian granulose cells, and the theca, the latter responsible for synthesizing and secreting progesterone, oxytocin and E2. These are essential hormones for regulating the estrous cycle and pregnancy sustenance in bovine cattle. After fertilization, corpus luteum development, follicular growth and progesterone concentration (>3.18 $nMol \cdot L^{-1}$), estradiol and oxytocin, influence embryo survival. Progesterone levels regulate immune responses by inhibiting the myogenic proliferation and activity of the lymphocytes. Additionally, they reduce the number of OXT receptors and block the release of PGF2α by the endometrium, and facilitates embryo development, and its production of Interferon-ĩ. These physiological events induced by the progesterone produced in the CL inhibit other physiological events that go alongside the luteal phase.

The role of the ovary

To sustain pregnancy, the existence of an active corpus luteum is required. The corpus luteum (CL) is the endocrine gland that develops from the ovarian granulosa and theca cells. These cells secrete progesterone, oxytocin (OXT) and the most important steroids that regulate the duration of the estrous cycle and are essential for the maintenance of pregnancy. These are essential hormones for regulating the estrous cycle and pregnancy sustenance in bovine cattle. After fertilization, corpus luteum development, follicular growth and progesterone concentration (>3.18

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nMol·L^{-1}), estradiol and oxytocin, influence embryo survival. Progesterone levels regulate immune responses by inhibiting the myogenic proliferation and activity of the lymphocytes. Additionally, they reduce the number of OXT receptors and block the release of PGF2α by the endometrium, and facilitates embryo development, and its production of Interferon-ĩ. These physiological events induced by the progesterone produced in the CL inhibit other physiological events that go alongside the luteal phase.

Role of the conceptus

In pregnant bovines, the presence of the embryo in the uterus modifies the manifestation of the luteal phase. This phenomenon depends on the capabilities of the conceptus to secrete a cytokine called trophoblastic protein (bTP-1) or (IFN-ĩ), which originates in the trophectoderm and is created during the reimplementation and elongation of the embryo between day 11 and day 24 after fertilization. This cytokine is responsible for inhibiting the maternal immune system and degrades the prostaglandin synthetase enzymes (PGHS), which catalyzes the conversion of arachidonic acid to prostaglandin (Khatib et al., 2010).

The role of the endometrium

The role of the maternal endometrium in the development of the luteal phase is characterized by the presence of the intracellular inhibitor of PGF2α(EPSI). This compound is present during almost all gestation. This indicates that the immune system response in the endometrium in pregnant females is depressed (Fair, 2016), and that antiluteolytic phenomena are predominant in early pregnancy, reducing PGF2α secretion, and facilitating pregnancy sustenance.

Factors related to pregnancy loss after artificial insemination and embryo transfer in female bovines

Non-fertilization and pregnancy loss in bovine cattle are conditioned by multiple factors (Ali, 2021), of which the following stand out: genetic factors (Molina-Coto, 2017); age (Duica et al., 2007; Osorio and Pedroso, 2021), weather (Hansen and Barron, 2011), nutrition (De Bie, 2017; Caton et al., 2020; Moriel et al., 2020), ooocyte quality (Morales et al., 2016); endocrine balance (Wathes and Lamming, 1995; Pankratova et al., 2019), uterine environment composition (Rizos et al., 2010), and other factors associated with assisted reproduction technologies and the epidemiological conditions of cattle (Warnick and Hansen, 2010). However, it should not be ignored that the sexual response is unique for every individual, and one factor can cause multiple reactions in each case; on the contrary, multiple factors can be the cause for one infertility issue.

Factors associated with the quality and efficiency of artificial insemination

Artificial insemination is a widely used technology by small, medium and large sized cattle producers for the implementation of inter-breeding and genetic enhancement programs. However, there are many biological, managerial and socio-economic factors that affect the quality and efficiency of the process, and this issue limits the participation of new users in some way. In this context, the Coordinated Research Project FAO/OEIA titled "The use of radioimmunoassay and related techniques to identify ways to improve artificial insemination programs in bovine cattle raised under tropical and sub-tropical climate conditions", was carried out for 4 years in 14 developing countries. This research assessed the following variables related to the physiological aspects of the cow: semen quality and the skills of the technician who applies the technology. The results are shown in table 1.

Table 1. Factors thant influence the efficiency and quality of artificial insemination services (Garcia et al., 2001).

Main Issue	Specific defficiency in AI	Affected population (%)
Inadequte AI due to wrong estrous detection		17.3
Own production	*AI in cows with corpus luteum	6.09
	*AI in cows not in the cycle	10.4
Defficient estrus detection and cattle manage	*Cows that fail to give birth, their subsequent estrous not detected, and that are empty when diagnosed for pregnancy	27.40 10.1
	* Cows that give brith, but lose the embryo and are empty when diagnosed for pregnancy	

According to this data, it became evident that the use of the standardized methodology in countries and the strategy of combining field data with progesterone levels (milk and/or blood) and the data bases, allowed the obtention of unique information about AI in developing countries. This researched allowed to identify the main factors that limit efficiency in the studied localities.

In this sense, the study showed that almost half of the issues in AI were due to human error. In this direction, further efforts should focus on alleviating the intensity of the discovered issues, with emphasis on the following: instruct cattle farmers on estrus detection, as well as animal management and nutrition practices; induction methods and estrus synchronization; improve the management, storing and quality control of semen; improve the registration, assessment and surveillance of inseminations.

Factors that influence pregnancy rate in conventional and *in vitro* embryo transfer programs

The conventional embryo transfer (MOET) and *in vitro* (PIE) programs are widely implemented due to the benefits they provide to genetic enhancement, gene conservation and biodiversity. The scientific literature emphasizes that pregnancy rates when implementing these technologies can go from 20 to 50%. This efficiency depends on the oocyte competence from the donors, the super ovulatory treatment procedures, the status of corporeal condition, the season, and the genotype. Similar aspects were found in donors reserved for PIE, in which the influence of the semen (sexed or non-sexed) and the cryopreservation methods were shown. In the receptors, the quality of the corpus luteum and its corporeal condition stand out (Osorio and Pedroso, 2021). In both groups (donors and receptors), the prevalence of inflammatory processes inside and outside the genital apparatus and the lack of micronutrients play a transcendental role, because the effects can be seen in the blood, the follicular fluid, and the uterine secretion content (Leroy et al., 2016; De Bie, 2017; Figueredo et al., 2017). Some of these results are shown in figure 1, with the recent findings in the implementation of this technology in the dry tropic climate of Ecuador.

These results suggest that, both the AI programs and embryo transfer require systematic control of its implementation. Moreover, within the scientific framework, it is necessary to continue researching the causes of oocyte competence, for maturation, fertilization and embryonic growth development. Similarly, environmental, nutritional and epidemiological factors can negatively influence the implantation and sustenance of pregnancy. These studies should focus on grazing cattle raised in tropical and sub-tropical climates. In this sense, research on molecular and cellular mechanisms during the biological phenomena can be attributed to the application of adequate biotechnological strategies that improve efficiency in artificial insemination and embryo transfer.

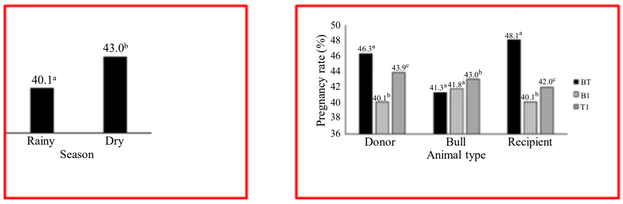

Figura 1. Factors that influence the pregnancy rate in female bovine rceptors of *in vitro* embryos in a lower tropical region of Ecuador (Osorio and Pedroso, 2021).

Impact of the epidemiological status of cattle

The epidemiological status of cattle is an important cause of failure in fertilization and pregnancy loss in cattle farming. Recent finding about the physiopathology of various infectious and parasitical diseases explain the mechanisms (molecular, cellular and endocrine) and how to apply adequate therapeutic measures in livestock production. In this context, mastitis (Dahl et al., 2017), pododermatitis, endometritis, hepatic fluke infestation and bovine viral diarrhea (Santos and Ribeiro, 2014; Bradford et al., 2015), are very common in livestock production in warm climates.

There are other infectious-contagious and parasitical entities that hinder reproduction, such as: trichomoniasis, campylobacteriosis, brucellosis, infectious bovine rhinotracheitis, ureaplasmosis, neosporosis, mycoplasmosis and tuberculosis. These entities are very common and well-known in warm climate livestock production. Consequently, there are specific control and treatment programs for these diseases (Salasel et al., 2010). Other non-specific inflammatory processes in the trachea, although not influential in the growth of pre-implanted embryos, do increase the number of cells in state of apoptosis (Fabian et al., 2010). Nonetheless, there has not been any studies that prove their association with embryo losses. Therefore, it would be appropriate to carry out research in this field, focusing on grazing cattle (Pedroso, 2011).

Procedures to diagnose pregnancy and predict embryonic losses in female bovines

Embryonic and fetal mortality are one of the inefficiencies in the reproductive process that cause a great part of economic losses in modern livestock production. These inefficiencies represent a deficit of 1 billion dollars worldwide per year. In this sense, studies on this issue have been on the rise in the last decades. In this context, research have focused on identifying the

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moment it is no longer viable, as well as embryonic and fetal mortality in vivo.

Recent findings have provided clear evidence of the critical periods of pregnancy loss. This has been possible thanks to available technologies that can identify fetal and embryonic mortality in female bovines (Wiltbank et al., 2016; Ealy and Seekford, 2018; Reese et al., 2020). Moreover, it was confirmed that the period whence embryonic and fetal mortality occurs is highly variable and is determined mainly by genetic factors, productive status, the environment and management conditions. The available procedures to diagnose pregnancy and the fetal and embryonic in female bovines are palpation and transrectal ultrasonography. These procedures are based on the accumulation of uterine fluids, the presence and size of the embryo or fetus, ovarian structures (CL/FO), and the growth of the placenta.

These techniques are used in pregnancy diagnosis. The former provides exact knowledge of the gestation stages between day 40 and day 60, and the ultrasound between day 25 and day 30 after artificial insemination or embryo transfer, although it is difficult to predict pregnancy loss. Regarding this, Doppler ultrasound constitutes one recent development in the area. With this tool it is possible to observe the blood flow in the blood vessels, and also to determine the blood flow in the uterus, the placenta, the corpus luteum activity and the stage of early pregnancy if the precise moments of estrus and ovulation are known (Herzog et al., 2010).

Moreover, to measure blood or tissue perfusion, that is, the flow of a fluid through a circulatory or lymphatic system, to an organ or tissue. But it is not enough to monitor the viability of the fetus or predict pregnancy loss, because the levels of progesterone can decrease at the same time the fetus' demise, or after (Scully et al., 2015; Pohler et al., 2016). For this reason, other procedures, such as ISG or PAG, are used (Melo et al., 2020).

Identifying progesterone (P4) in blood or milk is the most commonly used non-specific diagnostic method for pregnancy in modern livestock production. The difference in P4 levels between pregnant and non-pregnant females can be considered a sign of early stage gestation. As such, cows that show levels below (< 1 ng·mL^{-1}) between day 18 and day 24 after artificial insemination or embryo transfer can be classified as non-pregnant, and cows that show levels above (≥ 1 ng·mL^{-1}) during the same period can be considered non-pregnant, with 80 to a 100% accuracy when identifying non-pregnancy status. In this case, false positives can be attributed to long-lasting, persisting and cystic CLl and early embryonic mortality (Pohler et al., 2016). The high prevalence of false positives limits the use of this diagnostic method to show embryonic mortality.

The discovery of the specific glycoprotein associated with gestation in female bovine has also contributed to its use in diagnosing gestation viability and embryonic and fetal mortality. Thus, it has been proposed in recent studies that the pregnancy-associated glycoprotein (PAG) can serve as a biological sign of gestation and can predict late embryonic and fetal mortality, with 95% accuracy, after AI and ET. The PAG belong to the aspartic proteinase family. Many of the bovine PAG are produced by binucleated giant cells in the trophectoderm epithelium. With regards to this, a recent study aimed to identify the failures in gestations between day 30 and day 60 after AI or ET. Moreover, it was confirmed that the proportion of cows that experimented pregnancy loss was 23% (IATF) and 16% (FTFET), respectively (Greco et al., 2015).

However, it does not seem to be practical for many professionals due to lab resources it demands. Nonetheless, in order to identify embryonic mortality frequency, it is recommended to take a blood sample between day 22 and 24 to identify pregnancy and in between days 28 and 30 to identify embryo viability (Oliveira et al., 2020). The conceptus for the identification of pregnancy, and the implementation of the maternal uterus during the elongation involve the secretion of the interferon Tau and trophoblast protein (IFNT), which originates in the trophectoderm and is responsible for stimulating a group of genes (ISG) that attach themselves to the receptors at the surface of the cell (endometrium), initiating signaling pathways and the appearance of a sub-group of genes involved in the innate immune response system (mother).

In general, this gen commonly appears in response to a viral infection, but can also appear during a bacterial one or if there are parasites. In this case, its role is to modulate the rejection response from the maternal immune system to the presence of the embryo in the uterus. Then, it inhibits the secretion of prostaglandin and the sustenance of pregnancy. Generally, significant differences between pregnant and non-pregnant females have been found 18 to 22 days after AI or ET, with 70 to 90% accuracy (Ealy and Seekford, 2019; Melo et al., 2020). However, as it is shown, the great variability of these experimental results has limited its use in production. These variations may happen because the ISG genes can also respond to other types of interferons, such as those associated with certain viral infections (Shaw et al., 2017).

According to various studies, one of the most promising candidates in the search for biomarker of easy access to diagnose pregnancy are circulating microARN. But, for the moment, its use is limited to research activities, because of the lab techniques necessary to isolate them and measure them. According to experimental findings, between day 18 and 22 after AI or ET, these nucleoids play an important role in regulation the appereance of genes found in the uterine fluid, the amniotic liquid and in blood serum (Pohler et al., 2016). In this sense, thanks to the research, it has been possible to consider microRNA associated with pregnancy as candidates to identify pregnancy or the viability and mortality of the embryo. Cows that experiment an increase of miARN in day 17 to 24 after AI or ET have a higher rate of pregnancy compared to non-pregnant ones (Pohler et al., 2017). Nonetheless, there is still need to carry out new studies in order to achieve adequate repeatability and accuracy in the diagnosis, as well as the integrated use of reproductive management and pharmacological procedures.

During research on milking cows and double-purpose grazing cows under tropic and template climate conditions, various management systems were implemented to identify and induce a return to service in non-gestating to gestating status, known or unknown. These management methods, combined with identification of PAG, can be useful to carry out studies that can define pregnancy status, viability and mortality in embryos.

Biotechnical methods and strategies of reproductive management to improve female bovine fertility within artificial insemination and embryo transfer programs.

The acquired knowledge about sustenance mechanisms in pregnancy and embryonic development have allowed the introduction of modern methods to increase reproductive efficiency (Besbaci et al., 2020). In this sense, the energy supplement in diet stands out; vitamins, minerals and overflow fats (Ninabanda, 2018), the potential use of recombinant alpha interferon (Lenis et al., 2010), the pharmacological manipulation of follicular development and growth (Pedroso, 2011), the functions of the corpus luteum; the use of recombinant growth hormone (Hernández-Cerón and Gutiérrez-Aguilar, 2013). The development and optimization of fixed-time estrus, ovulation and AI synchronization methods (Lamb et al., 2010); progesterone supplementation (Mann, 2008) and the application of various methods of heat stress attenuation and nutritional status control systems (Schütz et al., 2014; Molina-Coto, 2017), genomic selection (Straden et al. ., 2019); supplementation and treatment with anti-oxidant substances (Greco et al., 2015; Pedroso and Roller, 2021).

Conclusion

Pregnancy loss is the main cause for longer intervals between births. Its three practical manifestations are: non-fertilization; embryonic or fetal mortality are the main indicators with the greatest negative impact in the productivity of cattle raising. This is multi-factor issue; thus, it is necessary to have deep knowledge of the physiopathology of identifying, implanting and sustaining pregnancy. The implementation of techniques for the manipulation of grown, development and atresia of the ovarian follicle; progesterone supplementation and Progesterone supplementation or the induction of accessory corpus luteum in the middle phase of diestrus in order to inhibit the luteolysis mechanism and enhance the functions of the CL are suitable procedures to improve the fertility of inseminated cows or after embryo transfer. . The main preventive measures are aimed at controlling the efficiency and quality of artificial insemination services and predicting the viability of the embryo after transfer. The application of these measures will allow for a sustained improvement in the effectiveness of assisted reproductive technologies.

Conflict of interests

The authors declare that they have no conflicts of interest in this publication in any of its phases.

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