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RELATIONSHIP BETWEEN METRITIS AND ANIMAL NUTRITION

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Abstract

Turkey is one of the leading countries of Europe in terms of animal existence. Today, yield per animal is important, not the number of animals. Reproduction is one of the indispensable items of dairy businesses. Most dairy cows do not achieve their reproductive performance goals, and economic losses occur at significant rates. The purpose of breeding cattle health is to ensure that cows become pregnant again until the best time after freezing and thus keep the time between the two raisins within economic limits. Reproductive performance is closely related to the baby's prenatal and postnatal health. Being pregnant again after birth is the most important factor for profitability. Immunosuppression is suppressed in long time, undernourished or stressed animals and the incidence of mastitis and metritis in animals is increasing. Economic losses due to this case take place. Considering the economic dimensions of these losses in our country, studies on 155 enterprises were made in Burdur, Kırklareli and Konya provinces. Within these studies, disease related loss was 1.258 turkish liras for clinical metritis, 697 turkish liras for retention.

Key words*: breeding, health, immunosuppression, metritis, reproduction.*

INTRODUCTION

Our country is one of the leading countries in the world in terms of animal existence. Today, the productivity per animal is important, not the number of animals.

Reproduction is one of the indispensable elements of dairy farms. In many dairy cows, reproductive performance targets cannot be achieved, significant economic losses occur. The purpose of reproductive herd health is to ensure that the cows become pregnant again in optimal time after calving, and therefore to keep the time between the two calves within economic limits. Reproductive performance is closely related to the health of the cow in the weeks before and after birth. The conception of the cow as soon as possible after birth is an indispensable factor for profitability (Kocaarslan, 2013).

The immune system is suppressed in animals that cannot become pregnant for a long time, malnutrition or under stress (Foldi et al., 2006) and the incidence of animals in cases such as mastitis and metritis increase (Görgülü, 2011). Economic losses occur due to these cases. Considering the economic dimensions of this loss in our country, studies were conducted in 15 enterprises in Burdur, Kırklareli and Konya provinces. Within the scope of these studies, the loss due to disease was determined as 1.258 TL and 697 TL per animal for clinical metritis and retentio secundinarum, respectively (Yalçın, 2008). The purpose of this review is to identify uterine infections, their causes, and their relationship to animal feeding.

POSTPARTUM PHYSIOLOGY AND UTERINE INVOLUTION

Processes for cows to conceive again after birth include uterine involution, regeneration of the endometrium, elimination of bacterial contamination of the uterus and resumption of cyclical activity of the ovary. Uterine involution; physical shrinkage, laxation of the karsts and regeneration of the endometrium (Sheldon et al., 2008). At birth, uterus weight is approximately 10 kg, whereas postpartum falls to 5 kg on day 6, 2 kg on day 12, 1kg on day 25 and 0,7 kg on day 50 (Öcal, 1997; Kocaarslan, 2013). Caruncula forms lochia flow and also contains blood from fetal fluids and broken umbilical veins in lochia (Figure 1). Initially endometrial regeneration occurs in the intercarpal region and then continues with the proliferation of cells to cover the sacrococcygeal regions (Sheldon et al., 2008)

The thickness of the cervix in uterine involution drops from 30 cm to 2 cm on postpartum day 7 cervix. Lochia is red brown in color and has no odor, sometimes is more fluid and yellowish-white. Postpartum day 14-23. the lochia is cut (Sheldon et al., 2008). In the first 15 days of cervical involution, the uterus is slower to involution and normally the diameter of the cervix is larger than the diameter in corns of uterus. Within 25-47 days of the postpartum, the cervix and uterine involution are substantially completed in terms of physical size (palpation-induced involution). A complete microscopic involution lasts longer and is resulted in around the day 25-50 postpartum. Although the physiological role of prostaglandin F2 alpha (PGF2α) within the first month of the postpartum is not clearly defined, it is believed that it plays a role in the induction of uterine contractions and thus contributes to uterine involution (Sheldon et al., 2008).

Figure 1. Normal lochia flow (Güler, 2015).

DIAGNOSTIC METHODS IN UTERINE DISEASES

Uterus; mechanically preserved anatomically by bacterial contamination by the vulva, vestibular sphincter and cervix (Bondurant, 1999). Immunologically, the defense mechanism consists of two parts, cellular and humoral. Cellular defense is largely composed of polymorphonuclear leukocytes (PML), and the humoral defense mechanism consists of globulins (Hussain, 1991). When bacteria reach the uterus, the most important part of the defense of the uterus towards bacteria is the nonspecific phagocytosis of neutrophil leukocytes (LeBlanc, 2008). Neutrophil leukocytes come to the inflammatory zone with the induction of various peptides produced by microorganisms in the inflammatory zone. Neutrophils come to the surface of tissues, cavities and microorganisms. During the periods when progesterone is dominant over the defense mechanism, the immunoreaction is reduced, whereas when the estrogen is dominant, the immunity is stimulated (Lewis, 1997).

PATHOGENESIS

The uterus is sterile before birth. During the birth and postpartum period, the cow's feces and skin are contaminated with bacteria from the surrounding environment and the uterus becomes contaminant (Sheldon and Dobson, 2004). During the first two weeks of the postpartum, the cow's uterus is in contact with a wide variety of bacteria ranging from 80% to 100% (Lewis, 1997; Azawi, 2008). The presence of uterine bacteria at this period is normal (Foldi et al., 2006). More than 90% of the cows are contaminating with uterine bacteria within the first 15 days after birth, while the rate of uterine bacterial culture gradually decreases within 2-4 weeks of the postpartum as the involution process progresses. On the 45th day after birth, this rate is 9% or less (Bondurant, 1999). In short, the bacterial contamination of the uterus in the first two weeks after birth does not necessarily mean that there is a clinical inflammation. That is, a distinction must be made between uterine contamination and uterine infections. Interstitial infection means the formation of the uterine-related disease following a series of events such as attachment of pathogenic bacteria to the mucosa, proliferation and colonization, penetration of colonized bacteria into epithelial tissue, and release of bacterial toxins (Sheldon et al., 2006; Azawi, 2008).

The postpartum uterine lumen environment promotes the multiplication of aerobic and anaerobic bacteria. Most of these bacteria contaminates the uterine lumen and then the bacteria are removed with the aid of the uterine defense mechanism. In addition, *Arcanobacterium pyogenes* (*A. pyogenes*), *Escherichia coli* (*E. coli*), *Fusobacterium necrophorum* (*F. necrophorum*) and *Prevotella spp.* Bacteria often play a role in the formation of uterine diseases. Indeed, *A. pyogenes, F. necrophorum and Prevotella spp.* it has been determined that they act synergistically to increase the likelihood of uterine disease. It has also been found that these bacteria increase the likelihood of clinical endometritis and the severity of infections. Numerically, the most common pathogens are *E. coli* and *A. pyogenes*. E. coli infections are already formed and provide the basis for A. pyogenes infections (Sheldon et al., 2008).

UTERINE İNFECTIONS

Metritis is uterine cavity, inflammation of the superficial and deep layers. Edema, leukocyte infiltration and myometrial degeneration are seen. Endometritis is only the endometrium, that is, the mucous membrane. If this involves inflammation; that is serosal perimetritis. If it also contains ligaments, it is called parametritis (Sheldon et al., 2006; Sheldon et al., 2008).

ACUTE PUERPERAL METRITIS

It usually occurs within 21 days following birth, and as shown in Figure 2, it usually occurs 4-10 days after birth (Foldi et al., 2006; Sheldon et al., 2006; Sheldon et al., 2006).

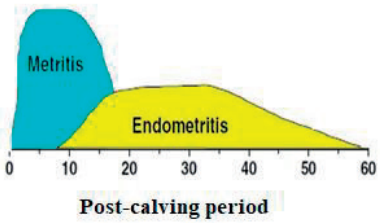

Figure 2. The period in which postpartum metritis species were active (Sheldon et al., 2008).

Acute puerperal metritis is characterized by a foul-smelling, watery uterine content with tissue rashes in it, enlarged and thin-walled uterus due to delayed involution, 39.5℃ fever, loss of appetite, stagnation, A. pyogenes, *E. coli* and *F. necrophorum, Bacteriodes spp., Provetella spp.* (Tuna, 2010) In the diagnosis of Puerpural metritis, rectal heat is observed in the first 10 days after delivery and a vaginal discharge is observed every 3 days until the postpartum day 21 is reached. The vagina make to be palpation. Vaginal discharge is mucopurulent, purulent, and putrified (Sheldon et al., 2004; Huzzey et al., 2007).

ENDOMETRITIS

Endometritis refers to the inflammation of the uterine endometrium layer. It is not deeper than the inflammatory in stratum spongiosum (Sheldon et al., 2006) and is the inflammatory response to all kinds of bacterial, viral, mechanical, thermal, chemical and toxic effects that affect the uterus itself. it is possible to mention many factors that cause endometritis and cause predisposition. Among these, dystocia, retention, secundinarum, and attempts to help birth follow infusion of irritant substances into the uterus (Youngquist, 1997). In vitro study, bovine herpesvirus (BHV-4) was claimed to play an important role in endometritis (Donofrio et al., 2007). Dystocia is an important cause of endometritis predisposition. First, the probability of retentio secundinarum and placental disposal is higher in those who have power delivery than in those who have normal birth (Table 1).

Table 1. Excretion times of postnatal membranes (Youngquist 1997).

Birth after	Membranes
Time, hour	**Excretion rates, %**
3	16.0
6	77.3
9	88.7
12	94.6
15	96.2
18	97.8
21	98.5
24	100.0

In addition, obstetric assistance and maternal tissue injuries during power delivery increase the incidence of uterine pathogens. Acute puerperal metritis is these factors that cause predisposition. also cause chronic endometritis in the healing process (Paisley, 1986; Correa, 1993; Noakes, 2001). In addition, inflammatory reaction leading to the separation of the caruncula and cotyledons in the postpartum period and lack of uterine contractions cause the placenta to be ineffective and thus endometritis (Guard, 1999). Microorganisms that cause endometritis often reach the uterus vaginally during mating, insemination or postpartum period. However, in some cases, transmission through the blood (hematogenous) may also be possible. In majority of cows, post-natal bacterial contamination of the uterus is mentioned, but in normal conditions this flora is rapidly eliminated. Endometritis can't perform uterine elimination of bacteria along with the inflammatory reaction of the endometrium in the shaped animals. Although the rate of bacterial contamination of the uterus is important in the development of endometritis, the pathogenesis of the disease is linked to the ability of the animal to eliminate infection rather than to bacteria (Kaya, 2008).

CLINICAL ENDOMETRITIS

Postpartum 21 days or more in the next days, purulent, mucopurulent exudates or is characterized by inflammation of the vagina. Cervical thickness is more than 7,5 cm at postpartum 21 days or after 26 days. In this time period, the vagina purulent uterine exudate is enough for diagnosis (Gilbert et al 2005, Sheldon et al., 2006). The most important symptom of clinical endometritis in cows is increase the enlarged uterus and vaginal discharge with cervix-wide (LeBlanc et al., 2002; Kasimanickam et al., 2004; Gilbert et al., 2005).

SUBCLINICAL ENDOMETRITIS

It is the inflammation of the endometrium without clinical symptoms and usually the uterine flow is not visible on the external side (Sheldon et al., 2006). In subclinical endometritis cows, there is a marked reduction in reproductive performance despite the absence of a clinical symptom (Sheldon et al., 2009). Endometriosis refers to an excessive infiltration of neutrophil leukocytes, and this increase can only be determined by endometrial cytology, not by the purulent structure of the cervical fluid (Foldi et al., 2006; Sheldon et al., 2006). The frequency of subclinical endometritis coincidence ranges from 37-74% (Sheldon et al., 2009), with a great deal of time depending on the time of diagnosis and postnatal transplantation. The main distinguishing feature between endometritis and metritis is that endometritis cows are not clinically disease (Güler, 2015). Subclinical endometritis is a major cause of infertility in cattle.

PYOMETRA

Postnatal functioning is a uterine inflammation characterized by accumulation of purulent or mucopurulent contents in the uterine lumen in the presence of a functional corpus luteum and its progesterone, and the resultant expansion of the uterine lumen (Sheldon et al., 2006). Although a functional corpus luteum is present, the cervix is not always fully closed and the pus flows mainly through the cervix to the vaginal space (Sheldon et al., 2006; Sheldon et al., 2008). Piyometra should be separated from clinical endometritis. The pylorus is less common than clinical endometritis. Pyometra is less than 5% less than the uterine clinical fever (Sheldon et al., 2008).

HIPOCALCEMIA AND METRITIS RELATIONSHIP

Postpartum period hypocalcemia causes dysfunction of bone, muscle and nerve tissue (Hayirli and Çolak, 2011). As shown in Grummer (1996), normocalcaemic cattle are more balanced in terms of energy balance and lower in concentration of NEFA than hypocalcemic cattle.

Subclinically hypocalcemic cattle have lower concentrations of neutrophils in the first 3 days of postpartum. The uterus health deteriorates due to the resulting immunosuppression. The incidence of metritis is parallel to the calcium concentration. Metritis has been reported development in 75.3% of hypocalcemia cattle (Martinez et al., 2012) (Figure 3).

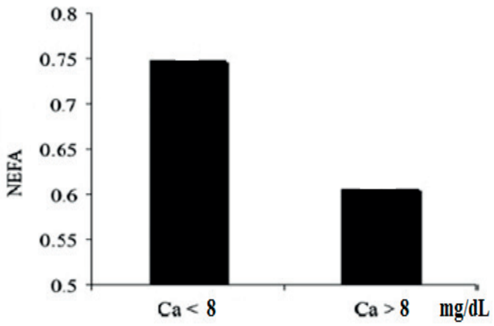

Figure 3. Calcium and NEFA between relation (Martinez et al., 2012)

RELATIONSHIP BETWEEN NUTRITION AND UTERUS HEALTH

In the periparturient period, negative energy balance arises if the energy requirement can't be met by feed consumption to meet body needs, growth of fetus and maintain lactation (Figure 4). Adipose tissue is used for energy needs, depending on the lack of enough energy source in the environment. Mobility of triglycerides in the adipose tissue results in nonesterified fatty acids (NEFA). In animals with high weight condition scores (WCS ≥3.5), the amount of nonesterified oil acid (NEFA) used to meet energy needs increased in circulation (Holtenius, 2003; Mashek, 2003; Arslan and Tufan, 2010). According to Theilgaard (2002), stressors such as epinephrine and norepinephrine increase lipolytic stimulation more as the amount of unfamiliar fatty acid (NEFA ≥ 0.6 mEq / L) increases (Ingvartsen, 2006).

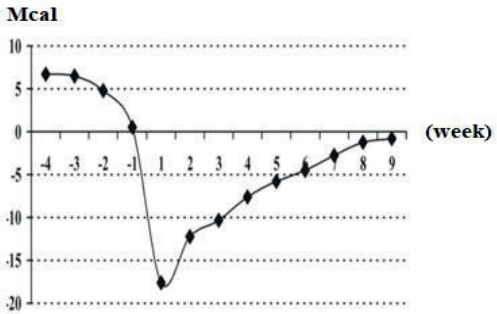

Figure 4. Peripartum energy balance
(Hayirli and Çolak 2011)

Approximately 50% of these fatty acids (NEFA) are oxidized to ketone bodies in the liver or re-esterified to triglycerides. Re-esterification of triglycerides and ketogenesis is carried out in hepatic tissue when NEFA is too abundant in the medium, and it is also converted to BHB, which is the predominant ketone body in a part of NEFA (Emery, 1992; Butler 2003). Since triglycerides can't be removed sufficiently by the liver as low-density lipoprotein (LDL), a significant portion is stored here (Rukkwamsuk, 1999). The increase in ketone bodies with the accumulation of triglycerides in the liver results in the formation of metabolic disorders such as fatty liver syndrome and ketosis. In addition, oocytes, granulose and immune cells undergo oxidative stress due to the high concentration of ketone bodies. Anovulation is prolonged due to negative energy balance (Hoeben et al., 1997; Suriyasathaporn, 1999; Bisinotto, 2012).

Increasing NEFA due to suppression of dry matter consumption in 2 weeks before birth and myeloperoxidase activity of suppressed neutrophils are associated with negative energy balance. The increase of both NEFA and BHBA in 2 weeks after birth may decrease the possibility of conception of the animal in early lactation (Hammon et al., 2006; Walsh et al., 2007; Ospina et al., 2010).

NEGATIVE ENERGY BALANCE AND HORMONAL BALANCE

Dairy cattle are hypo insulinemic in the early lactation period. The lower plasma insulin concentration in the mammary gland stimulates the increased oxidation of fatty acids and reduces glucose uptake and oxidation in insulin-responsive tissues (Butler, 2003). These hormonal changes lead to a decrease in dry matter consumption in the dry period and to the mobilization of fat deposits in postpartum period (Drackley, 2005; Ingvartsen, 2006). Insulin and Growth hormon-Insulin-like growth factor-1 (GH-IGF-1) play an important role in regulating metabolic activity during negative energy balance (NEB) of lactation in leptin and thyroid hormones (Chilliard et al., 2005). Negative energy balance (NEB) can delay ovarian activity by affecting the release of Luteinizing hormone (LH). When glucose and insulin levels decrease, it lowers the release of LH and limits the response of the ovary to gonadotrophins and endogenous opioids and other lactation hormones are provided by the inhibition of the pituitary gland of LH release necessary for the follicular development of the ovary (Butler, 1989).

Insulin-like growth factor-1 (IGF-1) is a factor affecting reproductive activity. IGF-1 is defined as a hormonal stimulant of pregnancy in cattle. It has been reported that IGF-1 significantly influences hepatic adaptation (carbohydrate and lipid) and many types of immune system during the transition period (Clark, 1997; Heemskerk, 1999; Van Dorland et al., 2009). The circulating levels of IGF-1 in the cows are gradually decreased in the subsequent lactation and lower during delivery to obtain maximum concentration during the uterine involution period. Cattle with endometritis produce less cytokines before inflammation. These cytokines are necessary for the inflammatory response and regulate the proliferation and function of the neutrophils in the infected uterus (Ahmadi et al., 2015).

OXIDANTS AND OXIDATION MECHANISM

Reactive oxygen species produced in excessive amounts in organism for any reason interact with nucleic acids, lipids, proteins, enzymes and carbohydrates, causing harmful effects resulting in cell damage and death. (Halliwell, 1993; Yerer and Aydogan, 2000). Free radicals make the most important effects on lipids. This effect is called lipid peroxidation. This reaction takes place continuously as a requirement of aerobic metabolism. Unsaturated fatty acids found in the cell membranes are the most susceptible to free radical damage due to the excessive number of double bonds (Kocaarslan, 2013). There is an increase in the amount of reactive oxygen species (ROS) in cows associated with the metabolic needs of pregnancy, labor and lactation, and this amount of ROS produced triggers stress due to oxidative oxidation in the animal (Sordillo, 2005). These ROS's initiate lipid peroxidation and start to damage the cells. In particular, the cells responsible for the immune system are much more susceptible to oxidative stress. Because their cell walls contain a high amount of polyunsaturated fatty acids (PUFA) and therefore they are much more susceptible to peroxidation. They also produce very large amounts of ROS at the same time when their immune cells are stimulated. The oxidative stress experienced during the transition period makes the animals more susceptible to other diseases. Dry matter consumption is significantly reduced in the few days before birth and the animal's immunity system is very weak (Kimura, 2002; Goff, 2006; Hammon et al., 2006). Alterations in the levels of sudden estrogen and progesterone during the last days of birth and a very serious increase in plasma cortisol levels during labor are another factor affecting the suppression of the immune system (Goff, 1997; Ingvartsen, 2006). Changes in the cellular level in the immune system occur (Mallard et al., 1998) and lymphocyte functions, antibody responses, cytokine production. (Cai et al., 1994, Kimura, 2002).

ANTIOXIDANTS AND TRACE MINERALS

Zinc, copper, selenium, manganese, molybdenum are micro-level substances essential to the body. Trace minerals are found at low levels in the tissues of the body. It is difficult to use in terms of skeletal development, immunological response and reproductive performance (Figure 5).

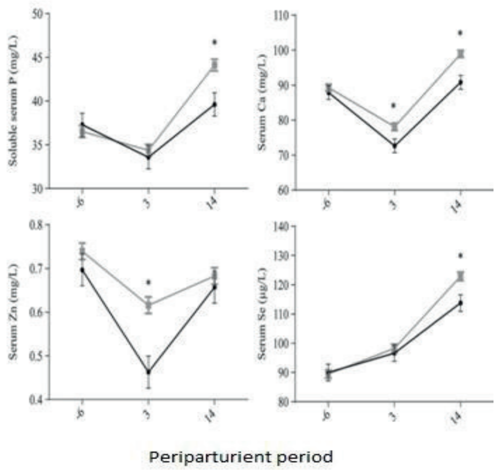

Figure 5. Concentration of trace minerals in endometritis and healthy cows in the periparturient period (Bicalho et al., 2014)

Zinc and copper serve as cofactors for components and enzymes of metalloenzymes. Enzymes that are copper chelated in cattle are important for survival (Underwood and Suttle, 1999). Xin et al. (Pogge et al., 2012) Zinc is one of the important elements for the health and growth of the animal. It has been reported that the neutrophils have a SOD (superoxide dismutase) and bactericidal capacity in the patients with copper deficiency (1991). Inadequate growth, deep anomalies, reproductive problems (Suttle, 2010).

During the transition period, the trace mineral consumption decreases due to the decrease in animal feed consumption. The alternative way of tracing mineral reinforcement is injection method. Induction of mineral traces of Cu and Se increased the concentration of liver by injecting 15 days of inception and increased the plasma concentration of Zn and Mn at several hours. In a study, 2 doses in the dry period were reduced with injections containing zinc, selenium, manganese and copper, as shown in table 2 (Machado et al., 2013).

Table 2. Percentage in relation to diseases of trace minerals used against uterine diseases (Machado et al., 2013)

Uterine Health	Control (%)	Micro mineral (%)
Dead birth	6.1	4.3
Endometritis	34.2	28.6
Metritis	11.5	11.8
Retensiyo Sekundinaryum	6.7	6.8
Abomasal displacement	2.6	1.3

VITAMINS AND OTHER SOURCES

Colostrum contains vitamin E and vitamin A at high levels. Ruminants in the postpartum period suffer from the inadequacy of these two vitamins by removing the colostrum (Goff, 2002).

In addition to changes in beta-carotene, vitamin A and vitamin E energy balance, vitamin sources that regulate antioxidant concentrations fall during birth (Goff, 2002). These vitamins play an important role in the immune function. Low concentrations of these vitamins are associated with suspicion of falling fertility and diseases in dairy cattle. Concentration of beta-carotene and vitamin E in circulation is lower in healthy cattle than in cattle with retention secondary cultures (LeBlanc et al., 2004).

ANTIOXIDANT EFFECT OF VITAMIN E-SELENIUM

Selenium deficiency is a negative effect on reproduction in all species. This problem has been widely reported in cows and sheep and selenium insufficiency is the direct cause of abortions, and selenium-related problems have increased susceptibility to diseases, and it has been stated that infertility is observed by complicating the excretion of the placenta. Vitamin E and selenium have been reported to complete involution in 8 days. Blood selenium flow was associated with high selenium in the ovary and this increase was reported to significantly increase GSH-Px activity in the follicular fluid and luteal tissue (Duraisamy, 2010). In animals fed vitamin E as feed additive, circulating NEFA and cortisol fall during frosting (Pontes et al., 2015). Addition of selenium and vitamin E increases the concentration of selenium in the serum and colostrum at the end of the dry period (Moeini et al., 2009). Vitamin E and selenium have also increased pregnancy rates in cows and sheep (Segerson, 1977; Segerson et al., 1981). According to Segerson (1981), this effect is attributed to the increase in sperm transport (Kocaarslan, 2013).

Addition of vitamin E and selenium to feeds reduces the incidence of retentio secundinarum (Segerson et al 1981). Arechiga et al., (1994) reported that a single prepartum injection of Vitamin E and selenium increased fertility. Vitamin E and selenium are reported to increase the incidence of juvenile dysplasia and have a positive effect on uterine health. Arechiga et al. (1998) reported that the number of inseminations per pregnancy decreased significantly in cows treated with vitamin E and selenium, and the pregnancy rate increased significantly.

Vitamin E and selenium are applied enough in well fed sheep and cows. Segerson (1977) suggested that selenium and vitamin E increase uterine contractions by affecting uterine muscle functions. In sheep, when vitamin E and selenium were applied, the fertilization rate was higher than the other group. In female sheep treated with vitamin E and selenium, the data of oestrus showed more total uterine contraction and more correct transduction in oviducts. Studies conducted in previous dairy cows suggest that selenium and vitamin E have a positive effect on reducing uterine muscle function and decreasing the incidence of retinococcal secretion (Duraisamy, 2010). Selenium, vitamin E and combinations of these have been reported to increase fertility in some studies (Segerson, 1977; Segerson et al., 1981; Arechiga, 1994), but not in others (LeBlanc, 2002), when assessed for fertility effects.

CONCLUSIONS

Metabolic changes in the puerperal period are negative for uterine health. There are applications to minimize the negative effect of these metabolic changes caused by negative energy balance on uterine health. In this period, glycogenic and lipogenic diets are recommended. The gluconeogenic adducts, including propylene glycol, glycerol and propionic acid, are glucose precursors and increase serum glucose concentration. Increased serum glucose concentration lowers fat mobilization due to increased insulin levels and low energy demand and thus increases reproductive efficiency in terms of uterine health. Glyconeogenic nutrient supplements have a stimulatory effect on insulin secretion. Propylene glycol appears to be a very effective glyconeogenic substance and reduces plasma NEFA and BHB concentrations. Propylene glycol and its metabolites stimulate insulin secretion.

Cattle feed consumption is low in early lactation and dietary fat supplement changes energy status in the early postpartum period. Increased caloric concentration with fat added to the ration improves the reproducible parameters. This improvement depends on the composition of the fatty acid. Polyunsaturated fatty acid (PUFA) positively affects the balance between the hypothalamus, pituitary and ovarian. Linoleic acid stimulates uterine involution (Gábor ve ark 2016).

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