Ovarian Cysts in Dairy Cows: Old and New Concepts for Definition, Diagnosis and Therapy

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Abstract

Ovarian Cyst (OC) is an important ovarian dysfunction and a major cause of reproductive failure in dairy cattle. Previously defined as enlarged anovulatory follicle like structures (<2.5 cm) and persisting for 10 or more days OC in dairy cows are currently defined as cystic ovarian follicular structures of at least 17 mm that persist for more than 6 days in the absence of corpus luteum. However, clear cut definitions of this disorder are yet to be made. Past evaluations of OC using transrectal palpations have increased, and accurate diagnosis currently employs a combination of transrectal palpation, transrectal ultrasonography and plasma progesterone assay. However, the accurate diagnosis of the type of OC seems less important as therapies are similar for both the types of OC and clinicians often evaluate the OC again under conditions of pregnancy failures. During earlier times, the manual rupture of OC was advocated, yet during the past several years single or combination hCG, GnRH, progesterone and prostaglandins have been frequent in clinical practice. Other therapies include estrogen receptor blocker clomiphene citrate and trans-vaginal ultrasound guided cystic follicle aspiration. Among the various therapies suggested the OvSynch treatment appears to be the most logical approach, yet the pregnancy rates with timed inseminations following therapy with the OvSynch treatment are low, as with other hormonal treatments. The success of therapy is governed by many confounding variables such as persistence of the cystic follicles and initiation of therapy as pathological alterations that occur following OC persistence require some time for spontaneous recovery. It can be concluded that OC can be diagnosed easily yet in spite of many therapeutic options the establishment of pregnancy in cows with OC requires a longer time.

Keywords: cows, CL, follicles, GnRH, ovarian cyst, ovsynch, ultrasonography.

Introduction

Over the past few decades milk yield per dairy cow has increased considerably due to continuing genetic selection and improvement of nutrition and herd management. Simultaneously with this selection for production characteristics, dairy cow fertility has declined significantly (Lucy, 2001; Butler, 2003). Economically, it is most beneficial if a cow calves each year (Dijkstraizen et al., 1997; Huinie et al., 2002). One of the most common ovarian dysfunctions during the postpartum period is formation of cyst following ovulation failure (Youngquist, 1986; Day, 1991b; Lopez-Diaz and Bosu, 1992; Laporte et al., 1994; Opsomer et al., 1998). Ovarian Cyst (OC) is a common and economically significant condition of dairy cattle (Johnson and Coates, 2004) affecting fertility. The condition was first described in the early 1900's and has been recognized as an important cause of reproductive loss in cattle. McNutt was probably one of the first to use the term “cystic” in referring to persistent follicles >20 mm in diameter (McNutt, 1927). In this manuscript we review the old and new concepts of definition, diagnosis and therapy for bovine ovarian cysts.

Definition

In the past OC were defined as fluid filled or hard structures of 2.5 cm or more in diameter persisting on the ovarian surface for 10 or more days (Roberts, 1971; Youngquist and Threlfall, 2007). The condition has been referred to by many names over the past century including adrenal virilism, nymphomania, cystic ovarian degeneration, cystic ovaries, and ovarian cysts (Garverick, 1997). Over time new definitions have been suggested, however, there is still lack of consensus and clearly defined definition. The condition is a consequence of a mature follicle that fails to ovulate at the appointed time of ovulation during the estrous cycle (Peter, 2004). Research using ovarian ultrasonography indicates that follicles typically ovulate at 13-17 mm in diameter (Ginther et al., 1989) so follicles that persist at that diameter or greater may be considered to be cystic (Hatler et al., 2003). Silvia et al. (2002) defined them as follicle like structures, with a minimum diameter of 17 mm and persisting for more than 6 days in the absence of a corpus luteum and clearly interfering with normal ovarian cyclicity. The diameter of the cyst may vary and reach up to 25 mm or larger (Roberts, 1971; Kesler and Garverick, 1982; Arbiter et al., 1990; Cook et al., 1991; Lopez-Diaz and Bosu, 1992; Boryczko et al., 1995; Fleischer et al., 2001; Silvia et al., 2002; Wiltbank et al., 2002; Youngquist and Threlfall, 2007). More recently, OC has been defined as anovulatory.
folicles (<2 cm) on one or both ovaries that fail to regress yet maintain growth and steroidogenesis and interfere with normal ovarian cyclicity (Vanholder et al., 2006). The absence of a corpus luteum is an essential OC criterion (Arbeiter et al., 1990).

The cyst may be present for less than 10 days (Arbeiter et al., 1990). On average, cysts are maintained for 13 days (Hamilton et al., 1995). Follicular turnover in cows with ovarian cysts takes 13 (Hampton et al., 2003) to 19 (Todoroki et al., 2004) days, whereas in clinically normal cows, it occurs every 8.5 days (Sirois and Fortune, 1988).

Cysts are often diagnosed in the absence of clear clinical signs, therefore the term “Cystic Ovarian Disease” no longer seems appropriate and should be replaced by the term “Cystic Ovarian Follicle (COF)” which does not necessarily implicate a state of disease (Vanholder et al., 2006). Non-steroidogenic cysts which are hormonally inactive do not influence the normal estrous cycle, so they can occur together with a corpus luteum. Therefore, recent research articles define COF differently and perhaps more logically (Hamilton et al., 1995; Gümen et al., 2002; Zulu et al., 2002; Hatler et al., 2003). In this review the condition is referred to as Ovarian Cyst (OC).

In most cases (62-85%), cows with luteinized cysts remain anoestrous (Day, 1991a; Watson and Cliff, 1997) as a result of the production of progesterone by luteinized cysts. Ball and Peters (2004) refer to these cysts as luteinized cystic follicles, describing them as cysts with thicker walls that produce high levels of progesterone.

Many researchers showed that OC are actually dynamic structures, which can regress and be replaced by new cysts (Kesler et al., 1980; Cook et al., 1990; Hamilton et al., 1995; Yoshioka et al., 1996). The factors that determine whether a cyst will regress or not, continue to be poorly known (Wiltbank et al., 2002; Peter, 2004).

**Diagnosis**

Diagnostic approaches for OC in cows include history and clinical signs, transrectal palpation, ultrasonography and plasma or milk progesterone assay. In the 1940’s, the presence of cystic follicles on the ovaries was mainly associated with nymphomania and a bull-like appearance in cows (Casida et al., 1944; Garm, 1949). Williams and Williams (1923) documented some of the physical signs associated with OC which include: loss of tone throughout the female genital tract, relaxation or stretching of the sacrosciatic and sacroiliac ligaments giving the raised tail head appearance, behavioral changes (buller cow) which are characteristic of nymphomania (i.e., excessive mounting, standing, and bawling with noticeably deeper tone) and erratic milk production.

The clinical signs that accompany ovarian cysts are variable. Anoestrus is most common, especially during the postpartum period (Kesler and Garverick, 1982). Irregular estrus intervals and development of masculine physical traits are other signs which may be present especially later during lactation (Roberts, 1971; Youngquist, 1986). It has also been determined that follicular cysts are anovulatory structures so, as long as they persist, cows will remain infertile (Youngquist and Threlfall, 2007). Nymphomania and irregular cycles are common (Kasari et al., 1996). Watson and Cliff (1997) detected OC during investigations for anoestrus (58%) and irregular heat (12%), at a negative pregnancy diagnosis (12%), and at a pre-breeding examination (17%). A proportion of cows with follicular cysts can also evidence regular estrous cycles but a lowered fertility. When follicular cysts persist for prolonged periods in dairy cows, endometrial glands hypertrophy and pathologies in the uterus many times culminate in clinical mucometra with normal estrous cycle lengths (Purohit, 2008). The presence of such cysts leads to an increase in calving-to-conception and calving intervals, resulting in significant economic losses in the dairy industry (Silvia et al., 2002; Isobe, 2007).

Due to many exogenous and endogenous factors, perturbation of the hypothalmo-hypophyseal-ovarian (HHO) axis results in anovulation (Peter, 2004). When compared to follicular cysts, luteinized cysts are more likely to persist over long periods of time and can lead to nymphomania in some animals (Ball and Peters, 2004). Ovarian cysts diagnosed after the puerperium had a negative effect on fertility, whereas when cysts are diagnosed during the puerperium they do not affect reproduction (Gossen and Hoedemaker, 2006).

The most likely time of diagnosis is 30-60 day after parturition in high-yielding dairy cows (Gordon, 1996) but the detection of anovulatory follicles during the first weeks after calving should not be considered an ovarian impairment. From a practical point of view, an ovarian impairment may be suspected when anovulatory follicles are detected no earlier than 7 weeks after calving, a time when reproductive functions are thought to be restored (Gier and Marion, 1968; Sheldon and Dobson, 2004).

Ovarian cysts and normal preovulatory follicles are differentiated on the basis of number and size but mainly on the basis of uterine tonicly (Bierschwal, 1966; Zemjanis, 1970). During transrectal palpation, ovarian cysts are identified as multiple follicles that are typically larger than normal ovulatory follicles with an increased overall ovarian diameter (Purohit, 2008) along with a flaccid uterus in the absence of a corpus luteum while cows in proestrus have an erect, turgid uterus (Bierschwal, 1966; Zemjanis, 1970). Differentiating ovarian cysts from deep postpartum nutritional anestrus is not difficult because cows in deep anestrus have low FSH secretion and small ovaries with minimal follicular development (Roche et al., 1992). OC are differentiated from shallow anestrus on the basis of the number and
size of the follicles, occurrence of follicular waves, body condition score (BCS), and stage of lactation (Bartolome et al., 2005).

Although transrectal palpation has long been the diagnostic approach, follicular cysts cannot be differentiated from luteal cysts solely by palpation (McLeod and Williams, 1991). It is difficult to distinguish between follicular and luteinized cysts without using ultrasonography in anoestrous cows (Jeffcoate and Ayliffe, 1995). The accuracy of diagnosing ovarian cysts and differentiating follicular and luteal cysts can be increased by combining transrectal palpation of the genital tract to determine that a corpus luteum is absent and the uterus lacks tone; ultrasonography to confirm that a corpus luteum is absent, to determine the size of follicles that are present, and to check for luteinization; and measurement of plasma progesterone concentration to determine the degree of luteinization (Bartolome et al., 2005). The accuracy of diagnosis can be increased by obtaining information about the reproductive history of the animal, vaginal examination and progesterone determination (Hanzen et al., 2000). Some cows may evidence normal estrous cycle although they may have one or multiple cysts in one or both ovaries.

Kahn (2010) described a luteal cyst as being characterized by enlarged ovaries with one or more cysts with thicker walls than those of follicular cysts because of a lining of luteal tissue. Ultrasonography is effective in detecting follicular and luteal cysts with high accuracy (Farin et al., 1990). Color Doppler sonography is superior to B-mode sonography for differentiating follicular and luteal cysts and aids in the selection of treatment (Rauch et al., 2008). However, exact prediction of OCs destined to regress or persist and the response of OCs to treatment with a GnRH analogue were not possible using color Doppler sonography (Rauch et al., 2008).

According to Bartolome et al. (2005), two approaches can be considered in the diagnosis of OC. First, detection of multiple follicles approximately 18 to 20 mm in diameter and second, ovarian follicular waves during a period of 7 to 10 days in the absence of ovulation, absence of corpora lutea, and a lack of uterine toxicity. Determining the presence of ovarian follicular waves during a 7 to 10 day period with follicles that reach ovulatory size (12 mm) can be used to retrospectively differentiate ovarian cysts from shallow nutritional anestrus with low BCSs (Bartolome et al., 2005).

In general, luteal cysts are associated with relatively high concentrations of progesterone in the peripheral circulation while follicular cysts are associated with relatively low concentrations of progesterone (Dobson et al., 1977; Farin et al., 1990, 1992; Jeffcoate and Ayliffe, 1995). Many researchers have used a plasma P4 concentration greater than 1 ng/ml as the minimum P4 concentration for a cyst to be considered luteal (Nakao et al., 1983b; Ax et al., 1986; Dinsmore et al., 1989; Jou et al., 1999; Santos et al., 2000). However, P4 limits above 0 ng/ml (plasma) and up to 10 ng/ml (milk) have been used (Farin et al., 1990; Nanda et al., 1991; Chavatte et al., 1993; Ribadu et al., 1994; Kasari et al., 1996). It should not be confused with hollow corpora lutea, which are not pathological at all (Garverick, 1997).

Thus accurate diagnosis of the type of OC requires a combination of diagnostic approaches such as transrectal palpation, transrectal ultrasonography and plasma progesterone profiles.

**Therapy**

The OC therapy appears to be simple however, regaining fertility, which often requires longer time due to perturbations in endocrinology and uterine pathology that follows in long standing cases (Purohit, 2008), seems to be more important. Treatments for OC are numerous and variable, and have changed considerably over the years (Roberts, 1986; Woolums and Peter, 1994; Peter, 2004; Purohit, 2008). Economically, the decision to treat an animal is influenced by the costs and the expected treatment benefits, the costs of replacement, and the breeding value of the animal (Bierschwal et al., 1975; Dinsmore et al., 1989; Scholl et al., 1992; Surisayathaporn et al., 1998; Jou et al., 1999; Douthwaite and Dobson, 2000). Many endocrine based treatments for cysts have been evaluated including steroids (Johnson and Ulberg, 1967), gonadotropins (Casida et al., 1944; Bierschwal, 1966; Bierschwal et al., 1975; Nakao et al., 1978) and GnRH (Bierschwal et al., 1975; Seguin et al., 1976; Kesler et al., 1978; Nanda et al., 1988). Some of the earliest treatments include: manual rupture, ovariecotmy, injection of ovarian extract, injection of CL extract, uterine infusions of antibiotics or antiseptics, and injections of adrenaline chloride and Pituitrin (Albrechtsen, 1917; Williams and Williams, 1923; Tutt, 1932; Casida et al., 1944). Roberts (1986) refuted ovariecotmy as a treatment option suggesting that spaying will correct nymphomania but the removal of only one ovary if it is affected with cysts is useless, since the remaining ovary will promptly develop cysts. According to Bartolome et al. (2005) differentiation is not always necessary for understanding the type of cysts because treatments under both conditions are similar. The success of therapy in terms of disappearance of OC with different hormonal treatments is good, yet the establishment of pregnancy requires variable times due to formation of new OC and pathological alterations that occur in the uterus with long term persistence of OC (Purohit, 2008). Many variables such as OC time of diagnosis, OC persistence period, presence of mucometra and milk production determine the outcome of therapy (Purohit et al., 2001; Purohit, 2008).
Spontaneous recovery

The spontaneous recovery percentage of early cysts is 60-65% (Kesler and Garverick, 1982; Refsdal, 1982; Day, 1991b). Arbeiter et al. (1990) and Purohit et al. (2001) found a spontaneous recovery percentage of OC in 27.17 and 24% of cows, respectively. Steinbauer (1985) recommended treatment only after day 50 post partum, because of possible spontaneous regression of the cyst. Youngquist (1986) stated that spontaneous recovery might reach 60% if the condition is present before 30 days post partum. It would be profitable to treat multiparous cows having cysts very early in the postpartum period, while treatment of primiparous cows should be delayed, at least until the end of the preservice period, to provide the opportunity for spontaneous recovery (López-Gaitus et al., 2002). Dinsmore et al. (1989) did not find major differences between clinical response to treatments given before or after 35 days post partum.

Manual rupture

In the past, manual rupture of OC had been suggested (Roberts, 1971) however, recently it has been mentioned that this method should be weighed against the cost of hormone therapy (Kahn, 2010). Brito and Palmer (2004) did not recommend manual rupture of cysts because it may result in trauma and hemorrhage causing adhesions and contributing to fertility reduction. Currently manual rupture of OC is not suggested due to potential dangers of hemorrhages and adhesions that may follow manual rupture (Purohit, 2008).

GnRH alone

The distinction between follicular cyst and luteal cyst is not important in practice, because the response of both types of cysts to GnRH treatment is similar (Youngquist, 1986; Dinsmore et al., 1989; Day, 1991b) and usually results in luteinization of the cysts followed by estrous within 4 weeks of treatment (Dinsmore et al., 1990). Cows with ovarian cysts are capable of releasing LH in response to GnRH (Cantley et al., 1975). GnRH is most effective for returning cows with anovulatory follicular cysts to a normal cyclic ovarian condition (Brito and Palmer, 2004). GnRH induces the release of LH, with a maximum plasma LH concentration being reached 90 to 150 minutes after application which initiates the formation of active luteal tissue, as indicated by increased serum progesterone levels 7 days after treatment onwards (Seguin et al., 1976; Kruip et al., 1977). In response to treatment with GnRH, ovulation of the cyst does not occur, but other follicles present at the time of treatment may ovulate (Brito and Palmer, 2004). GnRH had no effect on intervals from treatment to CL detection or from treatment to cyst disappearance, and that CL detection and cyst disappearance are not correlated; also there is no association between the gonadotropin response to GnRH and the interval from treatment to CL detection (Jou et al., 1999).

Thus, a single GnRH treatment has been the standard treatment for cows with ovarian cysts (Bierschwal et al., 1975; Seguin et al., 1976; Nakao et al., 1992; Osawa et al., 1995). However, a large proportion (25-39%) of cows with ovarian cysts treated with GnRH did not respond (Cantley et al., 1975; Nakao et al., 1992; Osawa et al., 1995; Tebble et al., 2001), probably because other follicles capable of responding to GnRH were not present (Tebble et al., 2001). Etherington et al. (1985) concluded that treating normal cows with GnRH in the early postpartum period may increase the risk of pyometritis and OC. It has been reported that following treatment with GnRH, OC may luteinize, but they never ovulate (Garverick, 1999). There is presence of a CL approximately 7 days after treatment with GnRH (Bierschwal, 1966; Ambrose et al., 2004) indicating that the CL formed from ovulation of an ovarian follicle, and not the existing ovarian cyst.

After the GnRH treatment and subsequent luteinization, the cyst becomes responsive to prostaglandin-F2α (PGF2α) because the steroidogenic synthesis pathway has switched from estradiol to progesterone. The newly elevated levels of progesterone are responsible for a restoration of responsiveness to the positive feedback effect of estradiol, resulting in the resumption of normal cyclic ovarian activity after the release of endogenous PGF2α and cyst regression (Brito and Palmer, 2004).

GnRH analogs

The epidural administration of lecirelin (a GnRH analogue) promotes the remission of follicular cysts and an improvement of reproductive parameters (Annalisia et al., 2011). A single intramuscular injection of buserelin at a dose of 10 μg or higher is recommended for the treatment of ovarian follicular cysts in cows (Nakao et al., 1992). A single injection of 20 μg buserelin and 200 μg fertirelin have equal therapeutic effects in lactating cows having OC (Osawa et al., 1995). Buserelin, a nanopeptide GnRH analog, is 10 to 20 times more potent than fertirelin acetate in eliciting the release of LH and FSH (Dinsmore et al., 1987; Chenault et al., 1990). The effects of either fertirelin or buserelin on the luteinization of follicular cysts and on subsequent reproductive performance are fairly well known (Nakao et al., 1980, 1983a, 1992; Dinsmore et al., 1987). In comparative studies, buserelin (a more potent GnRH analogue) or human chorionic gonadotropin (hCG) produced similar effects (Brito and Palmer, 2004). A recent study found beneficial effects of a single IM administration of 0.1 mg lecirelin acetate in the therapy of cows suffering from OC (Silva et al., 2012).
Since the 1970s hCG and GnRH analogues have been used to treat ovarian cysts, and both appear to be equally effective with regards to treatment response and fertility (Peter, 2004) but the next estrus would occur 5-21 days after treatment (Kahn, 2010). GnRH and hCG elicit equivalent endocrine and clinical responses, but GnRH has an advantage over hCG in its minimal antigenicity (Drost and Thatcher, 1992).

The treatment of OC with hCG is somewhat more effective than a treatment with hCG + P4 (Alanko and Katila, 1980).

**PGF2α**

Prostaglandin F2α (PGF2α) has been used for the treatment of luteinized cyst because of its luteolytic activity, and estrous symptoms can be observed within 2 or 3 days of treatment (Kesler and Garverick, 1982). It is the most effective treatment for luteinized cysts, and in one study, 75% of the cows were in estrus within 7 days after treatment and pregnancy rates at first estrus were 66% (Brito and Palmer, 2004).

Kahn (2010) recommended luteolytic doses of PGF2α as the ideal treatment for luteal cyst, with estrus being evident within 3-5 days. Intervals from treatment to resumption of ovarian activity are affected by the characteristics of ovarian cysts, with a faster recovery for the luteal type (Probò et al., 2011).

**Progesterone and progesterone implants**

Treatment with progesterone may disrupt the endocrine environment needed to maintain ovarian follicular cysts and thus lead to their regression (Hatler et al., 2006). At high doses, it exerts a strong negative feedback on LH pulse frequency (Kinder et al., 1996) which reduces LH in cows with cysts, and this was followed by development of normal ovulatory follicles (Calder et al., 1999). Acute treatment as well as chronic treatment (9-14 days) with progesterone caused a rapid reduction in the size of persistent follicles and restored cyclic ovarian activity (Johnson and Ulberg, 1967; Anderson and Day, 1994; McDowell et al., 1998; Calder et al., 1999). Cows with persistent follicles can be successfully synchronized and time inseminated using progesterone, GnRH and PGF2α but show a limited response to treatment with GnRH plus PGF2α (López-Gaitus et al., 2001).

Treatment with CIDR proved effective in restoring ovulation and reestablishing normal cyclicity in beef donor cows with cysts persistent for a long period (Douthwaite and Dobson, 2000). Insertion of a CIDR and GnRH injection in cows with follicular cysts can induce synchronous follicular wave emergence with the same pattern as observed in cows having normal estrous cycles (Kim et al., 2006). The CIDR reduces and maintains LH secretion at normal luteal levels, thereby, inducing atresia of estrogen-active cysts and preventing formation of cysts from the newly emerged follicles (Todoroki et al., 2001). Progesterone works against follicular cysts by restoring the responsiveness of the hypothalamus to the positive feedback of estradiol, resulting in normal estrus and ovulation within 7 days after the implant is removed (Brito and Palmer, 2004). Although the use of CIDR may eliminate the need for evaluation of the presence of a corpus luteum at the time of PGF2α treatment (Bartolome et al., 2005), the combination of both minimizes the risk of incorrect treatment and provides sufficient reproductive performance (Iwakuma et al., 2008). Progesterone and Estradiol Benzoate treatment administered using a PRID have a high rate of therapeutic effectiveness in cows with OC (Kim et al., 2004).

Moreover, when progesterone is used for estrus synchronization after embryo collection instead of PGF2α, the proportion of cows developing OC decreased from ~25% to <3% (Brito and Palmer, 2004).

**GnRH+CIDR**

Treatments of cows with OC with CIDR intra vaginal placement, GnRH followed by PGF2α 7 days later resulted in recruitment of new healthy follicles, synchronization of ovulation and resulted in a marked improvement in pregnancy rate (Amer and Badr, 2007). Treatments with progesterone releasing intravaginal devices (PRID) in combination with estradiol benzoate for 12 days evidenced therapeutic efficacy in resolving OC in post partum dairy cows (Kim et al., 2004). The effects with progesterone treatments were proposed to be mediated by restoration of the ability of hypotalamo-pituitary axis to generate an LH surge in response to an increasing estradiol (Todoroki and Kaneko, 2006).

**GnRH+ PGF2α combination**

Comparatively, ovarian cysts are less responsive to treatment with GnRH alone. GnRH plus Cloprostenol (CLP) 14 days later is effective in resolving cysts with significantly higher percentages of ovulation rates, returns to estrus, and pregnancy rates, and a much lower level of cystic persistence. It was previously suggested that more research be done on using different combinations of GnRH and CLP as treatments for OC in order to combat the problem to the fullest (López-Gaitus and López-Béjar, 2002). However, currently GnRH followed by PG 7-10 days later is a routinely used therapy for OC (Purohit, 2008).

**Ovsynch protocol**

Some recent protocols for synchronization of ovulation, commonly referred as Ovsynch, followed by
timed artificial insemination (AI) performed 16–20 h after the 2nd GnRH injection, yields pregnancy rates of about 25% in cows suffering from OC (Fricke and Wiltbank, 1999; Bartolome et al., 2000; Meyer et al., 2007). Stevenson and Tiffany (2004) used ov-synch protocol as a treatment for OC and found it to be effective in curing the cystic condition and got the previously cystic animal pregnant after AI. During the warm period, the pregnancy rates of the cystic cows were similar whether they received GPG or GPH treatment, during the cool period, there is a beneficial effect in using hCG at day 9 of the ov-synch protocol compared to GnRH on cumulative pregnancy rate (De Rensis et al., 2008). It appears paradoxical that high milk production predisposes to the occurrence of ovarian cysts, but that high-producing cows respond better to treatment compared to low-producing cows. It is hypothesized that the level of milk production on the day of cyst diagnosis could be an additional potential predictor of success of treatment of lactating cows with ovarian cysts using the Ovsynch protocol (Crane et al., 2006). The addition of CIDR to the Ov-Synch protocol had no remarkable effects on circulating plasma steroids and conception rates following fixed time artificial insemination in cows (Kawate et al., 2011).

Clomiphene citrate

It is an antiestrogen and may exert direct action on the pituitary gland to augment estrogen-induced LH release (Terakawa et al., 1985) so a dose of 300 mg of clomiphene citrate administered to cows after a 1% copper sulphate drench has been suggested for the treatment of OCs (Thakur et al., 1983).

Needle aspiration

Single transvaginal-guided needle aspiration of ovarian follicular cysts is an easy and good method for the treatment of follicular cysts. Moreover, it is a safe and good alternative method against the manual, active rupturing of cysts during trans-rectal palpation (Lievaart et al., 2006) but there is a tendency of the cyst to reform, and the difficulty in such a clinical condition lies not in the resolving of the cyst but in the attainment of a successful pregnancy, which is extremely difficult when cows develop clinical mucometra (Purohit, 2008). Regimens suggested to resolve mucometra include oral (3-10 gm of potassium iodide for 5-10 days; Bugalia and Kohli, 1981, 1983; Rajan et al., 1991; Purohit et al., 2001) or injectable administration of elemental iodide (McDonald et al., 1961) or uterine lavage (Prasithiphol et al., 1999).

Homeopathic drugs

Homeopathic remedies like homeopathic *Apis* (for the right side OC) or homeopathic *Lachesis* (for the left side OC) twice daily for 5 days, with either one being immediately followed by homeopathic *Natrum mur*; twice daily for three days are effective treatments for OC (Karreman, 2007). *Apis mellifica* is a common homeopathic medicine made from the female honeybee, while *Lachesis* is prepared from the fresh venom of the South American bushmaster snake and *Natrum mur* is made simply from sodium chloride, or table salt. If this treatment doesn't work, Heat Seek, a botanical herb blend typically used to enhance the observable signs of estrus, may be given as 10 tablets orally every other day for twelve doses (24 day treatment; Karreman, 2007). According to Rautha Filho and Bison (2009) the use of homeopathic medicines can’t be considered a source to study about homeopathic therapy due to its clinically and scientifically weak base.

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