Fertility parameters of dairy cows with cystic ovarian disease after treatment with gonadotrophin-releasing hormone

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Fertility data were collected every four weeks for 10 years from 40 herds of Holstein-Friesian dairy cattle. The data collected during 925 lactations from cows with cystic ovarian disease which were treated with 500 µg gonadorelin were compared with data from a control group of 13,869 normal lactations. The intervals between parturition and first insemination and between parturition and conception were significantly shorter (P<0·001) in the normal cows, but the interval between first insemination and conception was not. The overall conception rate tended to be higher (P<0·10) in the normal cows, but the conception rate after the first insemination was significantly higher (P<0·001) and the number of services per conception was significantly lower (P=0·008) in the normal cows.

CYSTIC ovarian disease is an important reproductive disorder in dairy cows. It is defined as the persistence of an anovulatory follicular structure with a diameter of more than 2·5 cm on one or both ovaries in the absence of a corpus luteum (Kesler and Garverick 1982, Lopez-Diaz and Bosu 1992), which results in a disturbance of reproductive function. Boryczko and others (1995) distinguished between follicular cysts, luteal cysts and intermediate cysts on the basis of the concentration of progesterone and oestradiol-17β in the cysts, and there is a broad variation in the number, size and type of cysts, resulting in a variety of clinical signs (Kasari and others 1996). Clinically, the disturbance of reproductive function is most frequently (62 to 85 per cent) characterised by anoestrus (Day 1991, Watson and Cliff 1997) caused by the production of progesterone by more or less luteinised cysts. However, nymphomania and irregular cycles are also quite common (Kasari and others 1996). It is not always easy to identify the type of cyst in an anoestrous cow (Jeffcoate and Ayliffe 1995), but this is not clinically important, because the response to treatment with gonadotrophin-releasing hormone (GnRH) is the same irrespective of the type of cyst (Dinsmore and others 1989, Day 1991).

The incidence of the condition varies between 5 and 30 per cent (Kesler and Garverick 1982, Lopez-Diaz and Bosu 1992, Laporte and others 1994, Hooijer and others 2001). The time at which a cow is examined in relation to calving is partly responsible for this wide variation (Opsomer and others 1996), because a substantial number of the cows which develop cystic ovaries re-establish ovarian cyclicity spontaneously (Kesler and Garverick 1982, Roberts 1986).

There are several treatments for cystic ovarian disease, including prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$), human chorionic gonadotrophin (hCG), GnRH and progesterone. $PGF^2{}_\alpha$ induces luteal cysts to regress, and signs of oestrus can be observed within two or three days of treatment (Kesler and Garverick 1982); hCG has luteinising hormone (LH) activity, and induces luteinisation; GnRH also induces LH release, and oestrus usually occurs within four weeks of treatment (Dinsmore and others 1990). Repeated treatments with GnRH at seven-day intervals give a higher rate of recovery than a single treatment (Eissa and El-Belely 1995). The administration of progesterone, via an ear implant or intravaginal device for nine to 10 days together with oestradiol induces the cyst to regress by suppressing its LH and follicle-stimulating hormone (FSH) support via a negative feedback mechanism. After the regression of the cyst, a new wave of follicles emerges (Roche and others 1997).

The most important parameter for determining the economic losses due to cystic ovarian disease is the interval between parturition and conception (Scholl and others 1992), that is, the sum of the intervals from calving to insemination and from insemination to conception; the interval from insemination to conception is increased if more than one service is required.

The aim of this study was to compare the fertility parameters of dairy cows with cystic ovarian disease which had been treated with GnRH from 30 days after calving with those of normal healthy cows.

MATERIALS AND METHODS

Herd characteristics

Forty Holstein-Friesian dairy herds in the northern Netherlands were monitored for 10 years according to a standard protocol; the study started in November 1986. Fertility data were collected every four weeks during herd health monitoring visits. Eighteen of the farms were visited by the same practitioner and the other farms were visited by six practitioners who all used the same protocol. In 36 of the herds, the animals were kept in loose housing with slatted floors, and in the other four they were kept in tie-stalls. Twenty-seven of the herds had between 25 and 75 cows and 13 had more than 75 cows.

Data collection

All the gynaecological findings and treatments were recorded in the veterinary automated management production control program for dairy farms (VAMPP) (Noordhuizen and Buurman 1984), and data were recorded from 19,440 lactations. From these were excluded: lactations during which the pregnancy diagnosis was unknown; lactations with a calving-to-conception interval less than 50 days and more than 250 days; lactations with an interval between calving and first treatment for cystic ovarian disease of less than 30 days or more than 170 days; lactations during which the treatment included medication other than GnRH; lactations in which the cow was not inseminated after treatment; and lactations in which the treatment took place on the day of insemination.

The following protocol was used to collect information about the fertility parameters. All the animals were investigated by rectal examination between 30 and 60 days after parturition. If they were not pregnant after at least three inseminations (repeat breeder), they were also examined. An animal was diagnosed with cystic ovarian disease if follicles with a diameter greater than 2·5 cm were detected on one or both ovaries in the absence of a corpus luteum; animals in

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which the condition was diagnosed were treated with 500 µg gonadorelin (Fertagyl; Akzo-Intervet) when they were diagnosed. Animals treated for the condition but not yet inseminated were monitored for a recurrence four weeks later and treated again if necessary. A rectal examination for pregnancy diagnosis was made between 40 and 70 days after the last insemination; and treated cows that were inseminated before the visit four weeks later were re-examined at the pregnancy diagnosis or as a repeat breeder.

Design and analysis

The data set was divided into two groups: 925 lactations of cows treated for cystic ovarian disease with GnRH, and 13,869 lactations of cows without the condition. These groups were compared with respect to the following variables: the interval in days between parturition and conception; the interval in days between parturition and first insemination; the interval in days between first insemination and conception for the normal group, and the interval between the first insemination after treatment and conception for the group with cystic ovarian disease; the conception rate (%); the conception rate (%) after first insemination; and the number of services per conception, that is, the number of inseminations per pregnancy.

When a herd was entered into the study in 1987, only data for cows which were pregnant were included in the dataset. The data from 1987 were therefore removed from the multivariate analysis of conception rate and conception rate after first insemination.

SAS (1989) and STATACORP (1997) software were used for the statistical evaluation. First, the significance of the difference between the groups with respect to conception rate, conception rate after first insemination and number of services per conception was analysed by using a chi-squared test. Because most classes with five or more inseminations contained fewer than five observations, these classes were combined for the chi-squared test. Secondly, to correct for possible confounding effects such as herd, parity, year of parturition and interval between parturition and first insemination, logistic regression was applied to conception (no/yes) and conception after first insemination (no/yes), with cystic ovarian disease as the main effect. Poisson regression was used to correct the number of services per conception for herd, parity, year of parturition and interval between parturition and first insemination and to estimate the incidence rate ratio (IRR) for the two groups. Biologically plausible interactions were tested. The model-building strategies for logistic and poisson regression were devised according to Hosmer and Lemeshow (1989). Plots of the Kaplan-Meier survival function (Kaplan and Meier 1958) were used to describe the time-related variables (the interval between parturition and conception, the interval between parturition and first insemination, and the interval between first insemination after treatment and conception). The log-rank test was used to compare the time-related variables of the two groups.

RESULTS

Descriptive results

After selection, the data set consisted of 14,794 lactations, including 925 for cows with cystic ovarian disease (6·3 per cent). However, only 817 cows were diagnosed with the condition because 82 were affected in two lactations, 10 were affected in three lactations, and two cows were affected in four lactations. In 854 of the lactations (92·3 per cent) the cows were treated once, in 66 (7·1 per cent) they were treated twice, and in five (0·59 per cent) they were treated three times.

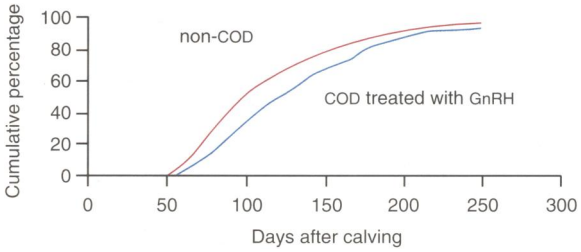

FIG 1: Cumulative percentages of normal cows and cows with cystic ovarian disease (COD) treated with gonadotrophin-releasing hormone (GnRH) which had become pregnant at intervals after calving

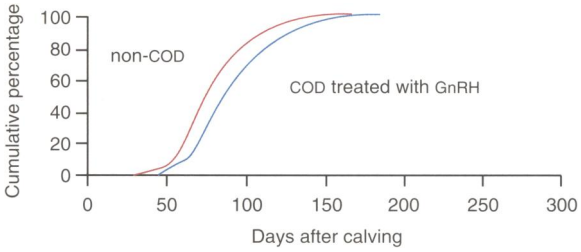

FIG 2: Cumulative percentages of normal cows and cows with cystic ovarian disease (COD) treated with gonadotrophin-releasing hormone (GnRH) which had been served at intervals after calving

Statistical analysis

The cumulative percentages of the cows which conceived in relation to days after calving were significantly different ($P<0·001$) for the two groups, with 50 per cent of the healthy cows having conceived after 96 days compared with 115 days for the cows with cystic ovarian disease (Fig 1). The cumulative percentages of cows which had been inseminated after calving were also significantly different between the groups ($P<0·001$) according to the log-rank test, with 50 per cent of the normal cows having been served after 77 days, compared with 89 days for the affected cows (Fig 2). Because both graphs are based only on the cows that conceived, the cumulative percentages both add up to 100 per cent. The interval between first insemination (in the affected group after treatment only) and conception did not differ significantly between the groups (Fig 3).

The results of analyses of the conception rate, the conception rate after first insemination and the number of services per conception are summarised in Table 1. The conception rates were 93·7 per cent for the normal group and 90·9 per cent for the affected group. In the univariate analysis the difference between the groups was significant ($P<0·001$), but in the multivariate analysis the difference was not significant ($P=0·053$). The conception rate after first insemination was significantly higher ($P<0·001$) in the normal group (51·1 per cent) than in the affected group (45·6 per cent). The effects of herd, year of parturition, parity and interval between calving and first insemination were significant ($P<0·05$) in both models for the conception rate and conception rate after first insemination. There were no significant interactions. Cystic ovarian disease tended to be associated with conception (observed ratio [OR] = 1·27) and it was significantly associated with conception after first insemination (OR=1·38). These results agree with the results of the chi-squared test.

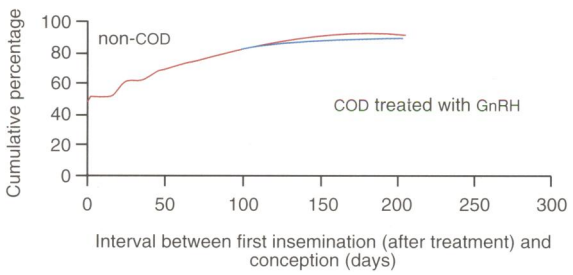

FIG 3: Cumulative percentages of normal cows and cows with cystic ovarian disease (COD) treated with gonadotrophin-releasing hormone (GnRH) which had conceived at intervals after first insemination

TABLE 1: Univariate and multivariate analyses of the conception rate, conception rate after first insemination and the number of services per conception of cows with cystic ovarian disease (COD) and normal cows

	Group	Number of lactations	Mean (%)	Univariate P value	Multivariate (OR/IRR)	95% CI
Conception rate	COD	925	90·9	<0·001	1·27*	0·97-1·62
	Non-COD	13,869	93·7			
Conception rate after first insemination	COD	925	45·6	<0·001	1·38†	1·20-1·58
	Non-COD	13,869	51·1			
Services per conception	COD	841	1·78	0·15	1·08‡	1·02-1·13
	Non-COD	12,995	1·72			

* P=0·053
† P=0·001
‡ P=0·008
OR Observed ratio, IRR Incidence rate ratio, CI Confidence interval

In the final model for the number of services per conception, the effect of cystic ovarian disease was corrected for herd and the interval between parturition and first insemination. The condition was significantly associated with an increased number of services per conception (IRR=1·08) (P=0·008). The correction for possible confounding effects thus changed the preliminary conclusions, based on the univariate analysis, with respect to the number of services per conception.

DISCUSSION

The fertility parameters of cows with cystic ovarian disease which were given one or more treatments with GnRH were compared with those of a large control group of cows. Matching the cows in the control group would not have been an acceptable alternative because too few cows would have remained after correcting for farm, season and calving pattern.

To be able to compare the results of similar studies of cystic ovarian disease, it is essential that the diagnosis of the condition is consistent. In this study, the diagnosis was made by experienced veterinarians by rectal palpation. They followed the protocol for fertility monitoring carefully and did not differentiate between follicular and luteal cysts, because it is not possible by rectal palpation alone and is not relevant in terms of the response to treatment (Dinsmore and others 1989, Opsomer and others 1998). Ultrasonography was not used because the technique was not available when the study began. The time after parturition when the cow is examined is critical if reliable results are to be obtained (Opsomer and others 1996). According to the standard protocol, the first examination was made from 30 days after calving, because the condition is common in cows shortly after calving and has a spontaneous recovery rate of nearly 60 per cent (Kesler and Garverick 1982). In exceptional cases, treatment was given less than 30 days after calving, but these lactations were excluded from the analysis. Lactations with treatments on the day of insemination were also excluded because these repeat-breeding cows were treated with GnRH to improve their fertility rather than to treat cystic ovarian disease. Culled animals were included in the dataset until they were culled, and, because the reasons for culling were either not evaluated or multiple in nature, the reason for culling was not included in the analyses.

The affected animals were treated with GnRH, which causes the release of endogenous LH (Youngquist 1986), luteinisation of the cyst and a recovery of normal cyclical activity (Hernandez-Ledema and others 1982). In a field study in the Netherlands, 50 per cent of cows treated for the condition with GnRH were inseminated within 24 days of treatment. More than 50 per cent of the cows which became pregnant after treatment needed only one insemination (Hooijer and others 1999).

The interval between parturition and conception is the sum of the interval between parturition and first insemination and the interval between first insemination and conception. Management factors, such as feeding and heat detection, play a key role in reducing the interval between parturition and first insemination (Brand and Guard 1996), because a negative energy balance and low insulin concentrations after calving may limit the responsiveness of the ovary to gonadotrophin stimulation (Butler and Smith 1989, Opsomer and others 1999). The interval between parturition and first insemination was longer in the group with cystic ovarian disease, but the interval between first insemination and conception was not. The prolongation of the interval between parturition and conception was therefore due to the prolonged interval between parturition and first insemination. Although the interval between first insemination and conception was not prolonged, the affected animals required more services before they conceived. This was probably because, unlike the insemination-to-conception interval, the number of services per conception was calculated by including all the inseminations before the first treatment. The same applies to the conception rate after the first insemination. The difference between the outcomes of the univariate and multivariate analyses in terms of the significance of the conception rate between the groups can be explained by the correction for the interval between parturition and first insemination in the multivariate analysis. It is difficult to compare the present results with those of other studies, because of differences in the numbers of cows included, the choice of treatment, the dosage, the time of treatment after parturition and the exclusion criteria. The results of this study show that the time at which cystic ovarian disease is diagnosed and treated after parturition is an essential factor in reducing the interval between parturition and first insemination, which in turn limits the economic losses caused by the condition.

Cystic ovarian disease prolonged both the interval between parturition and first insemination and the interval between parturition and conception. Furthermore, the cows with cystic ovarian disease required significantly more services per conception than the control cows. The treatment of the affected cows with GnRH did not increase the interval between insemination and conception after treatment. It is possible to limit the economic losses due to cystic ovarian disease by diagnosing and treating it sooner after parturition.

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Disseminated eosinophilic disease resembling idiopathic hypereosinophilic syndrome in a dog

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True idiopathic hypereosinophilic syndrome has been described in human beings and cats, but not in dogs. The syndrome is characterised by prolonged unexplained peripheral mature eosinophilia, the infiltration of many organs by eosinophils, organ dysfunction and a fatal outcome. This paper describes an idiopathic disseminated eosinophilic disease in a dog involving various organs, manly the heart and the lungs, accompanied by a leukemoid eosinophilic response, and a fatal outcome. The histopathological findings included the infiltration of the myocardium, lung parenchyma, liver, spleen, lymph nodes and skeletal muscles with eosiniphils.

THE idiopathic hypereosinophilic syndrome (HES) has been described in human beings and cats (Chusid and others 1975, Parrillo and others 1979, Fauci and others 1982, McEwen and others 1985, Harvey 1990, Neer 1991, Saxon and others 1991, Gallin 1994). Disseminated eosinophilic disease has also been described in a ferret and in two dogs. However, the ferret had a concurrent lymphoma, and both the dogs were infested by helminth parasites, which could have been the reason for the eosinophilia (Goto and others 1983, Blomme and others 1999). These cases do not fit the classic signs of HES which is characterised by a prolonged eosinophilia (eosinophils >1·5 x 10^9/litre) with no recognisable cause, organ dysfunction and often a fatal outcome. Many organs may be involved, including the heart, lungs, spleen, liver, blood, bone marrow, skin, gastrointestinal tract and nervous system (Neer 1991, Gallin 1994). The histological lesions consist mainly of the infiltration of tissues with eosinophils (Neer 1991, Gallin 1994). In human beings, cardiovascular lesions are present in approximately 84 per cent of the patients, predominantly in the left cardiac chamber (Davies and others 1983). In cats, cardiac lesions have been reported less frequently, and the main organs involved are the bone marrow, small intestine, mesenteric lymph nodes and the liver. A thorough search of the veterinary literature did not reveal a previous report of true HES in dogs. This paper describes a dog with idiopathic disseminated eosinophilc disease resembling HES, accompanied by a severe peripheral mature eosinophilia.

CASE REPORT

A six-and-a-half-year old intact male German shepherd dog had been depressed, anorexic, intolerant of exercise and list-

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