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Theriogenology

Different Therapeutic Approaches for Treatment of Cystic Ovarian Disease (COD) and its Effect on Conception Rate in Holstein Dairy Cows

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ABSTRACT

COD is an ovarian dysfunction and a major cause of reproductive infertility in dairy cattle. The objective of this study was to compare therapeutic approaches of COD in Holstein dairy cows and its effect on pregnancy/ artificial insemination (PR/AI). Those cows classified into 8 groups where 1stgroup (n=10) received (GnRH+hCG+PRID) , 2ndgroup (n=10) received (GnRH+hCG+PRID 2) , 3rdgroup (n=7) received (GnRH + hCG + CIDR), 4thgroup (n=46), received (GnRH+CIDR),5thgroup (n=10) received (GnRH+hCG), 6th group (n=19) received (GnRH) , 7th group (n=30), received (GnRH + PRID) and 8th group (n=10), received (GnRH + hCG + PRID1). Result revealed that differences in PR/AI among different treatment protocols were not significantly different (Chi square = 5.29, P = 0.63), where PR/AI in 8 groups was (50%, 50%, 57.14%, 50%, 30%, 52.63%, 66.67% and 40% respectively). In conclusion, the highest pregnancy rates numerically were achieved in cystic ovarian disease cows treated using single GnRH injection and PRID (66.67%), while the lowest pregnancy rates were reported in cows treated using GnRH and hCG (30.00%).

Keywords: *Pregnancy rate, COD, GnRH, Holstein dairy cows*

INTRODUCTION

Cystic ovarian disease is a reproductive problem that leads to increase calving intervals and increase calving-to-conception and resulting in a huge economic loss in dairy industry (Silvia *et al.*, 2002; Isobe, 2007).Ovarian follicular cysts are an anovulatory follicular structure 25 mm in diameter on one or both ovaries in absence of a CL for at least 10 days(Lopez-Diaz andBosu, 1992; Garverick, 1999).These cysts can be classified into two categories ,first one, is follicular cysts which characterized by fluctuant on palpation with thin wall and with irregular cycles and nymphomania are common signs (Kasari *et al.*, 1996). Secondly category is follicular luteal cysts which characterized by luteal tissue, hard on palpation and thick wall (Farin and Estill, 1993; Lopez-Gaitus *et al.*, 2002), with irregular cycles and Nymphomania are common signs (Kasari *et al.*, 1996).The ovarian cysts being replaced by new cysts or spontaneously recovered on the same or contralateral ovary after persisting for long time(Cook *et al.*, 1991; Hamilton *et al.*, 1995).Ovarian cysts diagnosed during examination of irregular estrus (12%) and anoestrus (58%)(Watson and Cliff, 1997).

The success of treatment of cysts depends on estrus detection and timed insemination in cows (Lopez-Gaitus *et al.*, 2002).The GnRH is used for ovulate the cyst or luteinized the anovulatory follicles (Gumen, 2003).In addition, luteolysis of these luteinized follicles by $PGF_2\alpha$ or a

combination of GnRH andPGF_2 α is efficient in treatment of cysts in dairy cows (Kesler *et al.*, 1978; Leslie and Bosu, 1983;Archbald et al. 1991; Gumen, 2003). Moreover, PGF_2 α is injected at 9-10 days following gonadotrophin treatment and the success of a protocol using GnRH-PGF2α rely on observation of estrus displayed by anovulatory cows within seven days after treatment with PGF2α (Gumen, 2003).

Several studies compared GnRH and PGF2α injections (7 days apart) to Ovsynch protocol without estrus detection (Stevenson *et al.*, 1999; Bartolome *et al.*, 2000) or a management herd system that depend on estrus detection a.m/p.m service and periodic using of PGF2α (Pursley *et al.*, 1997). Several reports on using Ovsynch protocol for treatment ovarian cysts in dairy cows (Bartolome *et al.*, 2000; Pursley *et al.*, 2001; Cordoba and Fricke, 2002; Gumen, 2003; Crane *et al.*, 2006; De Rensis *et al.*, 2008a and 2008b) with conception rates of 24 to 35%.

The progesterone can be used as therapeutic approach for ovarian cyst in dairy cows and the conception rate following using PRID is 21% (Zulu *et al.*, 2003), CIDR is 27.3% (Bartolome *et al.*, 2005). While, Bartolome et al. (2005) attained 37.3% pregnancy rate in cows with cysts treated by CIDR-synch. However, Kim et al. (2006) obtaining a conception rate 52.3% during using CIDR + Ovsynch program. In the contrary, (Youngquist and Threlfall, 2007) reported that no significant difference between CIDR-synch program and ovsynch protocol during treatment of cystic ovarian disease.

Therefore, the aim of the present study was to treat cases of COD by using different therapeutic approaches and comparing their efficacies in Holstein dairy cows.

MATERIALS AND METHODS

Animals

The current study was carried out on a total of 142 mixed parity Holstein dairy cows (lactation number ranged between1and7)in a well-managed private Holstein herd (Umer dairy farm, Sheikhupra, Pakistan) during the period from (January 2018 to March 2019). The average daily temperature ranged between 16 and 25 ^{o}C while monthly fluctuations of relative humidity ranged from 20 to 40%. All animals were proven free from any infectious and contagious diseases and were routinely vaccinated according to a scheduled vaccination program. Animals were fed a totally mixed ration (TMR) according to nutrition research council recommendations (NRC, 2001).

Reproductive examination

Cows(n=142) were diagnosed with COD by rectal palpation and ultrasonography using portable scanning device supplied with a linear trans-rectal probe using the B-mode with 6-8 MHz frequency (SonoscapeA5). Animals should be divided into the following groups based on treatment options as shown in Table (1). Their average age was 4.5 years, average lactation was 2.37 lactation, and their average production was 32.1-liter milk.

Experimental design

The 1st group was cows (n=10) received 5 ml GnRH (Renceptal, busrelin acetate 0.004 Selmore company), 5000 IU hCG (IVFC, Galaxy pharma company + intravaginal application of PRID DELTA-1 (previously used one time for 7 days) (progesterone 1.55 gm, CEVA) for seven days **(Van Wervenetal., 2013)**.

The 2nd group was cows (n=10 cows) received the PRID DELTA-2 (previously used 7 days for 2 times) (PRID® DELTA is an intravaginal progesterone releasing device made of ethyl vinyl acetate and polyamide which contains 1.55 g progesterone Ceva Santé Animale, France).

The 3rd group was cows (n=7 cows) received the same treatment as the 1st group with replacement of PRID DELTA-1 with CIDR (progesterone 1.38 gm, Pfizer) for seven days.

The 4th group was cows (n=46 cows) received only GnRH + CIDR **(Crane *et al.*, 2006)**

The 5th group was cows (n=10 cows) received only GnRH + 5000 IU hCG.

The 6th group was cows (n=19 cows) received only 5 ml GnRH.

The 7th group was cows (n=30 cows) received 5 ml GnRH + PRID DELTA (new not used before)

The 8th group was cows (n=10 cows) received 5 ml GnRH, hCG and once used PRID.

Mating and pregnancy diagnosis

All cows were inseminated at detected estrus with frozen-thawed semen from approved sires. Ultrasonographic diagnosis of pregnancy was carried out on day 35 after insemination to determine conception rate according to Kasimanickam, et al. (2018).

Statistical analysis

Data were statistically analyzed using SPSS

statistical program, version 27. (SPSS, 2020). ANOVA was carried out to determine the differences among means at P<0.05. In addition, variations in PR/AI among different treatment protocols was tested using chi square test. Overall, a p value less than 0.05 was considered significant.

Table (1): Effects of different treatment options on pregnancy rate per artificial insemination in dairy cows suffering from cystic ovarian disease.

G	Group	Insemi nated	Pregnant	PR/AI	AV. LACT	AV.DIM	AV.TBRD	AV.MILK
1	**GnRH+hCG+PRID**	10	5	50	2	198	3.2	35.6
2	**GnRH+hCG+PRID2**	10	5	50	2.2	198	3	35.4
3	**GnRH+hCG+CIDR**	7	4	57.14	2.7	195	1.8	32.4
4	**GnRH+CIDR**	46	23	50	2.1	240	3.5	27.4
5	**GnRH+hCG**	10	3	30	3.8	254	4.1	35
6	**GnRH**	19	10	52.63	2.47	234	3.4	33.3
7	**GnRH+PRID**	30	20	66.67	1.6	305	2.9	27.7
8	**GnRH+hCG+PRID1**	10	4	40	2.1	239	3.2	30.2
AV		142	74	52.10%	2.37	233	3.1	32.1

Table 2: Effects of different treatment options on pregnancy rate per artificial insemination in dairy cows suffering from cystic ovarian disease.

Group	Inseminated	Pregnant	PR/AI (%)
GnRH+hCG+PRID	10	5	50
GnRH+hCG+PRID2	10	5	50
GnRH+hCG+CIDR	7	4	57.14
GnRH+CIDR	46	23	50
GnRH+hCG	10	3	30
GnRH	19	10	52.63
GnRH+PRID	30	20	66.67
GnRH+hCG+PRID1	10	4	40

Differences among different treatment protocols were not significantly different (Chi square= 5.29, P = 0.63).
GnRH: Gonadotropin releasing hormone; hCG: Human chorionic gonadotropin; CIDR: Controlled internal drug release; PRID: Progesterone releasing intra-vaginal device; PRID1: PRID used once; PRID2: PRID used twice; PR/AI: Pregnancy rate per artificial insemination.

Fig.1: Ultrasonographic image of Holstein cow ovaries showing (A) large follicular cyst (B) large double follicular cyst.

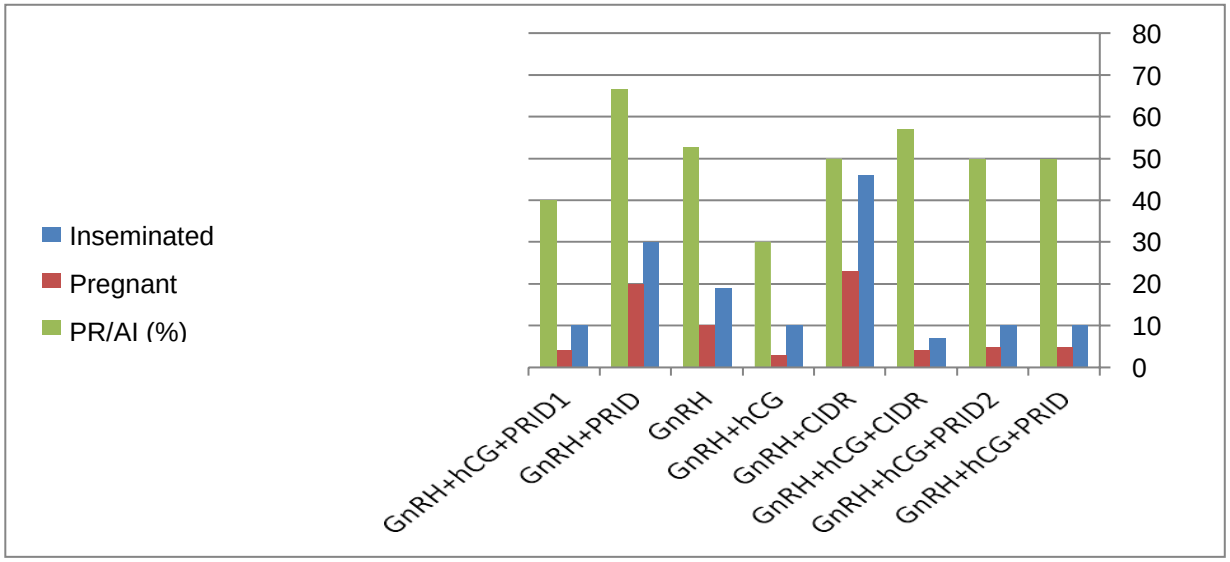

Fig.2: Effectsofdifferenttreatmentoptionsonpregnancyrateperartificialinsemination in dairy cows suffering from cystic ovarian disease.

RESULTS

Ultrasonographic characteristic of ovarian cysts revealed that the cysts were large, thin walled structure and non-echogenic as shown in Fig. (1).The PR/AI in dairy cows suffered from cystic ovarian disease according to treatment option and based on data, no statistical differences were observed among different treatment options (Chi square = 5.29, P = 0.63) as shown in Table (2). The PR/AI in cows received GnRH as a treatment was 52.63%. Combined treatment with GnRH and hCG resulted in 30% PR/AI. In addition, 50% of cows treated with GnRH plus CIDR conceived. For cystic cows treated using a combination of GnRH, hCG and CIDR, PR/AI was 57.14%. Accounting for PRID based treatments, combined treatment of cystic cows with PRID and GnRH yielded the numerically highest PR/AI (66.67%). The use of PRID, Once used PRID and twice used PRID in combination with GnRH and hCG resulted in PR/AI 50, 40 and 50%, respectively as shown in Fig. (2).

DISCUSSION

In the current investigation, no significant variations in PR/TAI were observed among cattle groups receiving different therapeutic approaches for cystic ovarian disease. The numerically highest pregnancy figures were observed in cows treated using GnRH and PRID (66.67%). The numerically lowest pregnancy figures were observed for cows treated using GnRH+hCG. It should be noted that pretreatment determination of cyst type has not been carried out in this study, thus planned treatment based on cyst type had not been performed. The second issue of concern in this experiment is that available previous history about cyst occurrence during the fresh period in animals under trial is lacking. These two actions might have been responsible for the obtained results. Coinciding with our results, combined treatment of cystic ovary in cows using a PRID and GnRH has resulted in 60% pregnancy rate in a study by Nanda et al. (1988). The authors reported that this treatment combination had led to 68% of treated cows resumed normal cycles with or without display of estrus.

In fact, Literature states that GnRH as a single treatment of cystic ovary in cattle does not need to know the type of cyst as both types of cyst respond similarly to treatment where the cyst would luteinize and be followed by estrus within 4 weeks of treatment as depicted by Dinsemore et al. (1990).It seems likely that ensuing estrus occurs due to the response of ovarian follicles that present on the ovary at time of cyst treatment, meanwhile the cyst itself does not ovulate but luteinize in response to GnRH treatment. It was, hence, recommended that a single GnRH treatment of ovarian cyst in cattle is a standard treatment (Osawa *et al.*, 1995).

Compared to GnRH alone, combined treatment

of ovarian cyst using GnRH and hCG resulted in lower pregnancy rates in cows in our work. This finding partially agrees to the findings obtained in a previous work by Alanko and Katila (1980) but disagrees to the results in some studies which demonstrated that both GnRH and hCG are equal in their effectiveness to treat cystic ovaries in cattle (Peter, 2004 and Khan, 2010). It is likely that antigenicity of hCG might have been responsible to limited success as a therapy of ovarian cyst (Frost and Thatcher,1992).

When comparing PR/AI in cystic cows treated by GnRH plus different local sources of progesterone, it was found that GnRH+PRID protocol gave better PR/AI (66.67%) than GnRH+CIDR (50.00%). CIDRs and PRIDs have been repeatedly used as effective therapies against cystic ovaries in cows **(**Nanda *et al.*, 1988). Van Werven et al. (2013) concluded higher pregnancy figures with PRID, compared to CIDR in dairy cows similar to the finding we obtained, but treated cows were not suffering from ovarian cystic conditions in their work. In that study, authors found that circulating progesterone in treated cows was significantly higher after PRID administration compared with CIDR. Linking higher progesterone during the period of follicle development prior to insemination with higher pregnancy figures might be the actual cause of higher PR/AI in cystic cows treated with GnRH+PRID, since PRID was documented to confer higher progesterone levels which are essential for proper follicle development and conception. We speculate that GnRH caused maturation of a concurrent follicle with the cyst while providing cystic luteinization, the follicle matured in an environment rich in progesterone might possesses oocyte of greater developmental potential and consequently future embryo with much higher opportunities to establish pregnancy (Van Werven *et al.*, 2013).

Different hormonal combinations with PRID resulted in nearly comparable pregnancy rates in cystic cows, thus, for economic reasons, using GnRH+PRID can be strategically used in the treatment of ovarian cysts in cattle to obtain satisfactory results.

CONCLUSION

This study revealed that the highest pregnancy rates were achieved in cystic ovarian disease cows treated using single GnRH injection and PRID (66.67%), while the lowest pregnancy rates were reported in cows treated using GnRH and hCG (30.00%),

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Conflict of interest

The authors declare they do not have any conflict of interest.

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