تأثير بعض العلاجات الدوائية على الأداء التناسلي لأبقار اللبن في فترة ما بعد الولادة

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EFFECT OF SOME HORMONAL TREATMENTS ON THE REPRODUCTIVE PERFORMANCE IN EARLY POSTPARTUM DAIRY COWS

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INTRODUCTION

The reproductive status of a dairy herd has a large bearing on production profitability. Reproductive problems resulting excessively long lactations or long dry period or both. Both are costly to dairy producers **(Grusenmeyer and Hillers 1989)**. Uterine diseases and ovarian dysfunctions are big reproductive problems cause a decrease in reproductive performance in dairy cows. Indeed epidemiological studies of dairy herds supported this association between uterine diseases and ovarian dysfunctions. Uterine diseases are associated with slower growth of ovarian follicles and their function is compromised as judged by reduced estradiol secretion. This disruption of ovarian functions is likely to further compromise fertility and reduce conception rates **(Sheldon, Williams, Miller, Nash, and Herth, 2008).**

The general goals for postpartum reproductive health in dairy cattle are for uterus to become completely involuted and free of infection , and for cows to be cyclic by the time they enter the postpartum breeding period (after 50 to 60 days in milk). The out comes of reproductive performance are the occurrence of pregnancy, normal time from calving to conception, and reasonable number of inseminations **(Ferguson and Galligan, 2000).**

Many management practices and environmental factors influence the reproductive performance of a dairy herd including estrus defection efficiency, age, nutrition, body condition score, semen handling techniques, transition cow management, calving difficulty, metabolic health, udder health, cow comfort, stocking rate and heat stress **(Lucy , 2001).**

Poor reproductive performance reduces income and profitability through its effects on several areas of herd performance. Long calving intervals result in more milk lactation but less milk per day of life when calving intervals are long, fewer calves are born each year, culling due to reproductive failure increases and low conception rates resulting in higher semen costs, often associated with higher veterinary bills. Extended periods of low production and long dry periods often result in an increased incidence of fat cows.

The common fertility parameters used to measure reproductive performance are days to first observed estrus, days to first insemination, days open (Calving to conception interval) , number of services per conception and conception rates (first service conception rate , first two services conception rate and first three services conception rate).

Several studies were conducted in view to improve the reproductive performance in dairy herds. Some of these studies were carried out to investigate influence of application of some managemental procedure as use of heat detection aids or heat detection methods to improve the reproductive performance. However, other authors studied the effect of some nutritional programs or certain mineral, trace elements or vitamin supplement on fertility of the animals.

On other hand, many researchers investigate influence of different methods for estrus synchronization and control of ovulation on reproductive performance of dairy cows. While, other authors investigate influence of administration of some hormonal treatments immediately after parturition (within few hours after calving) or in a period of

postpartum anoestrus on measured fertility parameters. The results of the effect of these hormonal treatments on fertility parameters were conflicted among the previous reports.

Therefore, the present work aimed to study,

1. Effect of treatment of normal parturient dairy cows with prostaglandin F2 alpha, ergometrine, oxytocin or estradiol benzoate immediately after calving (within two hours) on the following fertility parameters: days to first observed estrus, days to first insemination, days open , number of services per conception, first service conception rate, first two services conception rate and first three services conception rate .

2. Influence of treatment of normal parturient dairy cows with GnRH at day 14 postpartum on reproductive performance monitored by previously mentioned fertility parameters.

3. Effect of treatment with estradiol benzoate at 12 hours after parturition followed by injection of oxytocin 6 hours later on reproductive performance of postpartum dairy cows monitored by measuring of fertility parameters.

4. The work will present a comparison between the fertility parameters following each treatment and those in non treated animals (control) and among the treatments.

CONCLUSION

Days to first observed estrus was significantly increased in cows which received estrogen followed by oxytocin compared with those in non treated cows (control) or animals received GnRH, PGF2 alpha, ergometrine, oxytocin or estrogen.

Days to first insemination was significantly longer in cows that received estrogen followed by oxytocin than those in non treated cows (control) and treated with GnRH, PGF2 alpha, Ergometrine or Oxytocin. However, administration of estrogen was significantly decrease the days to insemination in treated animals compared with those in non treated (control) and treated animals with other previously mentioned treatments.

Days open in cows which received ergometrine or estrogen followed by oxytocin was significantly longer than those in cows received no treatment, GnRH, PGF2 alpha or oxytocin. However, it was significantly shorter in cows which were administered estrogen than those in non treated animals and in treated animals with other treatments.

The only significant effect on number of services per conception was observed in cows which injected with ergometrine. It was significantly higher than those followed administration of other treatments and non treated animals. A significant improvement in first two services conception rate was demonstrated after administration of estrogen while injection of ergometrine caused significant lowering in first three services conception rate. Non significant difference in the first three services conception rate was found between cows treated with estrogen or GnRH and non treated cows. However, the administration of PGF2 alpha, ergometrine or estrogen followed by oxytocin decreased the first three services conception rate compared with this in non treated animals. This decrease was tended to be significant statistically.

Generally, an improvement in the reproductive performance was occurred after administration of small dose of estradiol benzoate (5 mg) immediately after parturition. While, insignificant effect was noted after administration of GnRH, PGF2 alpha or oxytocin on days to first observed estrus, days to first insemination, days open and number of services per conception. Detrimental effect and significant decrease in reproductive performance was reported following administration of ergometrine or estrogen followed by oxytocin.

Dedicated to

My family,

My mother,

My oldest brother,

My wife

and

all who shared or help when are needed.

DISCUSSION

Aim of the present work was to study effect of administration of GnRH at day 14 postpartum and PGF2 alpha, ergometrine, oxytocin, and estrogen immediately after parturition or estrogen at 12 hours postpartum followed by oxytocin at 6 hours later on fertility of dairy cows. The fertility was evaluated by measuring the following fertility parameters: Days to first observed estrus, days to first insemination, days open, number of services per conception, first service conception rate, first two services conception rate, and first three services conception rate.

Effect of administration of gonadotrophin releasing hormone on fertility of postpartum dairy cows:

Previously, it was reported that administration of GnRH on day 14 postpartum to lactating dairy cows resulted in a surge of blood LH, ovulation and establishment of regular estrus cycle **(Britt et al., 1974)**. LH and FSH levels reached peak during 30 to 60 minutes and return pre injection concentration within 4 hrs **(Kaltenbatch, Dunn, Kizer, Cora, Acbar, and Niswender 1974; Kesler et al., 1977)**. Surge of LH in dairy cows also resulted from injection of GnRH from 10 to 15 days after calving **(Fernandes et al., 1978)**.

Similarly, **Chanault et al. (1990)** reported that GnRH induced effects indirect through release of LH and FSH. Results of **Ireland, Milvae, Martin, Atin, and Behrman (1990)** indicated that GnRH will not have direct stimulatory or inhibitory effects on corpus luteum. **Thatcher et al. (1993)** reported an acute increase in the rate of uterine involution was associated with induction of ovulation during the week following administration of GnRH.

Results obtained from the present study indicated that a decrease of mean of days open by 27 days and mean of days to first insemination by 14 days in animals treated with GnRH than those in control. Despite the difference in days to first observed heat and days open between treated cows and non treated controls, the difference was statistically non significant .

Non significant differences in other fertility parameters (Days to first observed estrus, Services per conception, and conception rate) were found between treated and non treated cows. It was concluded that no effect for injection of GnRH at day 14 postpartum on fertility of dairy cows. Our data agree with those obtained by **(Britt et al., 1975; Manns and Richardson, 1976; Britt et al., 1977; Webb et al., 1977; Lishman et al., 1979; Langley and Ofarrell, 1979; Nash, Ball, and Olson 1980; Etherington et al., 1984; Cavestany and Foote, 1985; Stevenson and Call, 1988; Mattos et al., 2001)**. **Manns and Richardson (1976)** found non significant difference between treated and control for interval from parturition to conception as well as **Langley and Ofarrell 1979 (1979)** demonstrated that GnRH administration at day 14 postpartum did not influence reproductive performance. Similarly, **Nash et al. (1980)** observed no effect on fertility in cows received only 100 mcg GnRH.

Two reports **(Etherington et al., 1984; Cavestany and Foote, 1985)** indicated that no pro fertility effects of GnRH given early postpartum. As well as, **Stevenson and Call (1988)** reported that no beneficial effects of the treatment with GnRH were detected

on any measurement of fertility regardless of pueperium classification. Also, **Britt et al. (1975); Webb et al. (1977), and Lishman et al. (1979)** reported that the life span of GnRH induced corpus luteum was generally less than 14 days and cyclic ovarian activity usually did not ensue. Similarly, no significant difference between GnRH treated and control for interval to first insemination, interval to conception and services per conception was observed by **Britt et al. (1977).**

Contrary to the results of present study, several studies have demonstrated that administration various doses of GnRH between day 10 and 18 postpartum improved various parameters of fertility in dairy cows, including decreased interval from calving to conception **(Peche, 1979; Nash et al., 1980; Benmrad and Stevenson 1986; Aboul-Ela and El keraby, 1986; Labib et al., 1988; Archbald et al., 1990)** and lower services per conception **(Peche 1979; Nash et al., 1980; Riek,1982 Benmrad and Stevenson, 1986; Aboul-Ela and El keraby, 1986; Labib et al., 1988)**, increased conception rate (**Nash et al., 1980; Lee et al., 1983)**, and decreased days to first estrus and ovulation **(Peche, 1979; Abou-Ela and El keraby 1986; Labib et al., 1988; Bechett and Lean, 1997)**.

Some authors suggested that the improvement of fertility of GnRH treated animals was owing to accelerate rate of uterine involution **(Britt et al., 1974; Fernandes et al., 1978; Thatcher et al., 1993; Foote and Rick, 1999)**, and the others mentioned that the improvement was due to stimulate ovarian activity **(Schams et al., 1973; Britt et al., 1974; Britt et al., 1975; Deaver et al., 1977; Kesler et al., 1977; Fernandes et al., 1977; Foster, Lamming, and Peters, 1980; Zaied et al. 1980; Brown and Reeves, 1983; Peters et al., 1985; Peters and Lamming, 1986).**

On contrary to results of the current study and data obtained by all previously authors, **Etherington et al. (1984)** observed that GnRH administration on day 15 postpartum increased incidence of pyometra and pre breeding anestrum. In same direction, **Mattos et al. (2001)** noted that administration of GnRH implants was able to suppress follicular growth, reduce the concentration of estradiol, corpus luteum development and concentration of progesterone in postpartum cows and subsequently may decrease the fertility or cause no effect. The adverse effect of GnRH on fertility which reported by **Mattos et al. (2001)** may be attributed to use of method of GnRH administration (implant) which was different than methods of administration used by other authors or due to other factors linked by condition of experimental animals throughout the study .

The variation in the results among authors might be due to many factors which influence the response to GnRH treatment as physiological state of the animal at the time of injection, energy balance of postpartum cows, ovarian status and other endocrine and environmental effects.

Effect of prostaglandin F2 alpha administration immediately after calving on fertility of dairy cow :

Prostaglandin F2 alpha increased after the end of parturition to reach peak values within 3 days postpartum and did not return to basal levels until 15 days **(Edqvist et al., 1980).** Nearly similar results were obtained from data of **(Lindell et al., 1982),** they found long uterine involution times were associated with insufficient synthesis of PGF2

alpha and they also added that the concentration of PGF2 alpha remained high for a longer period after calving in which the uterus involuted more rapidly. On other hand, PGF2 alpha has been shown to reduce the incidence of sub clinical uterine infection and hasten the return to a suitable uterine environment for fertilization and pregnancy **(Ott and Gustafsson, 1981)**. Therefore, the current study was planned in view to investigate the influence of PGF2 alpha administrated immediately after calving on fertility parameters of dairy cows. Our hypothesis was based on PGF2 alpha has an uterotonic effect (ecbolic) and may accelerate uterine involution or has a lutealytic effect on corpus luteum of pregnancy which may induce early increase in estrogen / progesterone ratio and consequently increase genital tract defence mechanism and consequently increase fertility of the cow.

Contrary to our expectation, the present results revealed that no effect resulted from administration of PGF2 alpha immediately after parturition on fertility measurements except first three services conception rate was tended to be significantly lower (72.22%) in treated cows compared with control (100%). The values of days to first observed estrus, days to first insemination, days open and services per conception in treated animals were appeared to be equal to control and there is no any significant difference between them. Many studies were conducted to evaluate the fertility of cows after administration of PGF2 alpha between day 3 and day 50 postpartum but we had not available literatures talked about the injection of PGF2 alpha immediately after parturition and its effect on fertility of postpartum cows. So, unfair to compare the present results with results of the previous studies, which administrated PGF2 alpha in the period of postpartum but not immediately after parturition.

Previously, PGF2 alpha was administered at day 3 to 13 postpartum twice daily **(Lindell and Kindahl , 1983)**, day 14 to 28 postpartum **(Young et al., 1984)**, day 20 to **24 (Benmrad and Stevenson, 1986)**, day 11 to 25 postpartum **(Stevenson and Call ,1988)**, day 10 to 14 postpartum **(Youngquist, 1988)**, day 14 to 16 postpartum **(McClary et al., 1989)**, day 8 postpartum **(White and Dobson,1990)**, day 50 postpartum **(Kristula, Bartholomew, and Galligan, 1992)**, day 21, 34, 57 postpartum **(Risco et al., 1995)**, day 25 to 30 and 39 to 40 postpartum **(Pankowski et al., 1995)**, day 12 postpartum **(Schofield et al., 1999)**, and during the first three weeks postpartum **(Elsheikh and Elzubeir, 2005) .**

Improvement in reproductive performance was reported in the majority of studies. This improvement was monitored by decrease days open (**Benmrad and Stevenson, 1986; Lucy, et al., 1986; Youngquist, 1988; Risco et al., 1995; Michiel et al., 1999; Heuwieser et al., 2000; Elsheikh and Elzubeir, 2004)** or high conception rate **(Young et al., 1984; Young et al., 1986; Stevenson and Call, 1988; Pankowski et al., 1995; Michiel et al., 1999)** or decrease of number of services per conception **(Benmrad and Stevenson, 1986; Schofield et al., 1999)** or stimulate the early cyclicity **(Zimjanis, 1980; Risco et al., 1995; Schofield et al., 1999; Heuwieser et al., 2000)** or accelerate the uterine involution **(Lindell and Kindahl, 1983; Elsheikh and Elzubeir, 2004)**. Irrespective of the time of administration of PGF2 alpha, results obtained from this study were not consistent with previously mentioned results that reported that injection of PGF2 alpha postpartum improved the fertility in dairy cows.

If we postulated that the effect of PGF2 alpha administration was the same regardless the time of postpartum administration, results of some authors (**Cooper, 1974; Hafs, Manns, and Drew, 1975; Olson, 1980; Elmarimi, Gibson, Morrow, Martenui, Gerloff, and Melancon, 1983; Richardson et al., 1983; Mortimer, 1984)** were consistent with data of the present work. They concluded that no improvement in fertility of cows after injection of PGF2 α in the postpartum period.

In agreement with current study, recent study of **Hirsbrunner, Burkhardt, and Steiner (2006)** indicated that the administration of PGF2 alpha or a combination of PGF2 alpha and PGE2 at 21 to 35 days postpartum had no beneficial effect upon measured fertility variables except a tendency to shorter interval from calving to first insemination. In another recent research **(Mejia and Lacau-Mengida, 2005)** reported that reduction in conception rate in primiparous cows was occurred after postpartum administration of PGF2 alpha which agreed with our data. While the same treatment caused improvement in fertility in multiparous cows monitored by reduction in the interval from calving to conception.

From the available literature there was only one study **(White and Dobson, 1990)** reported that administration of PGF2 alpha had an adverse effect on fertility of dairy cows. It reduced the occurrence of first estrus and increased the interval from calving to conception. These results were controversial to our finding and results of other authors that indicated that PGF2 alpha administration improved the fertility of postpartum dairy cows.

Effect of administration of ergometrine immediately after calving on fertility of dairy cows :

Ergometrine and ergonovine have been known to posses oxytocin activity by stimulating uterine smooth muscle **(Saameli, 1978; Rall and Schlefer, 1980; Kao, 1989)**. Powerful oxytocin and vasoconstrictive effect of ergometrine malate on the postpartum uterine activity was also reported (**Sloss and Dufty, 1980)**. From previous studies, we hypothesized that postpartum administration of ergometrine in dairy cows would stimulate uterine contractility and accelerate uterine involution, and therefore, a positive effect on fertility was reported.

Contrary to our hypothesis, the results of the current research revealed that there is no effect of ergometrine injection immediately after calving on days to first observed estrus and days to first insemination. However, marked significant extension in the days open from 180.93 ± 27.56 in control to 249.64 ± 39.34 in treated animals with ergometrine and significant increase in the number of services per conception from 2.00 ± 0.22 controls to 4.29 ± 0.79 in treated animals was observed. First service conception rate and first two services conception rate were lower in treated animals than control but this decline in conception rate was significant in first three services conception rate of treated cows (57.14%) if compared with those of control. It was clear from the present results that the adverse effect of ergometrine administration on fertility of treated postpartum dairy cows.

In the present study, incidence of retained placenta after ergometrine administration was not recorded. Three researches **(Zaiem et al., 1994; Eissa, 2003; Hussein and Metwelly, 2004)** were conducted to study the effect of injection of ergometrine (Methergin) directly after parturition on the incidence of retained fetal membranes and subsequently reproductive performance. They found a decrease in the incidence of retained fetal membranes and an improvement in the reproductive performance; these data were not consistent with our results.

Ergometrine was used by two authors **(El-Azab et al., 1988; Peters and Laven, 1996)** for the treatment of retained fetal membranes. **Peters and Laven (1996)** reported that it stimulate uterine contraction and aid in the expulsion of membranes while, **El-Azab et al. (1988)** reported that ergometrine was not effective for expelling retained fetal membranes .

Obviously, ergometrine administration immediately after parturition in the present study caused marked decrease in the fertility monitored by significant lowering in conception rate, increase in days open and increase in services per conception. The suggested reasons for the adverse effect of ergometrine injection immediately postpartum on fertility in dairy cows may be causes related to hormonal disturbances following ergometrine injection which resulted in disturbances of reproductive function or may be attributed to lowering of defence mechanism (local immunity of the genital tract) .

Reproduction function in cows is governed in part by LH, FSH and PGF2 alpha, plasma prolactin and LH concentration were lowered and most cows exhibited secretory PGFM responses after ergot alkaloid treatment **(Browing et al., 1998)**. They also noted that reduced LH concentrations as a result of ergot alkaloids associated with endophyte infected fescue may contribute to poor reproductive performance in cows by altering of luteal function.

The effect of ergometrine on fertility in the present work was similar to those reported by **Porter and Thompson (1992); Powell and Petroski (1992); Porter (1994), and Paterson, Forcherio, Larson, Samford, and Kerley (1995)**. They demonstrated that ergot alkaloids associated with endophyte infected tall fescue lowered reproduction rates in cow herds by unknown mechanisms. **Browning, Thompson, Sartin, and Browning (1997) and Browning et al. (1998)** reported an altering of hormones (LH, FSH, Prolactin, and PGF2α) following injection of ergometrine or ergonovine **(Browning et al., 1998)** or feeding of ergot alkaloid infected tall fescue **(Browning et al., 1997).**

Detrimental impact of ergometrine injection immediately after parturition on fertility of dairy cows in the present study and some other studies indicated that the disadvantages of ergometrine as reproductive toxin (altering the endogenous hormones ,LH , FSH, PGF2α, and prolactin) overcame its advantages as stimulator for uterine contraction and vasoconstrictive, the later effect may be beneficial for women and some species of animals for the different nature of their uteri than uterus of cows . However, vasoconstrictive effect of ergometrine early after parturition in cows decreased blood flow to the uterus and consequently decreases transportation of the humeral and cellular

immunity to the uterus and in turn decreases local immunity of genital tract particularly the uterus which needs more blood supply to increase and maximize the host defence mechanism.

Effect of injection of oxytocin immediately after calving on fertility of dairy cows

It is generally believed that oxytocin induced contraction of smooth muscle of the uterus **(Eiler et al., 1984)**. We hypothesized that administration of oxytocin immediately after calving would stimulate uterine contractility and accelerate uterine involution and consequently improve the fertility. The results of the current study have shown that, no significant effect for oxytocin administration on days to first observed estrus, days to first insemination, days open and number of services per conception. However the first three services conception rate was tend to be significantly lower (68.75%) in treated animals than in control (100%).

The relationship between oxytocin and ovarian activity cited in some studies, in early research **(Armstrong and Hansel, 1959)** concluded that concentrations of exogenous oxytocin may have been too low to alter function of the anterior pituitary. **Fletcher (1973)** demonstrated that frequent injection of oxytocin (5 iu) given ten times daily during the first 17 days postpartum shortened the interval to first estrus and first ovulation in ewes. **Convay et al. (1983)** suggested that hormones released at suckling may depress gonadotrophin secretion and/or inhibit ovarian activity. In same direction, **Goodman and Grosvenor (1983)** reported that oxytocin released by the pituitary in response to suckling or milking stimuli might affect gonadotrophin secretion. **Stewart and Stevenson (1987)** indicated that physiological doses of oxytocin alone do not inhibit establishment of postpartum ovarian activity.

There is a relationship between oxytocin and PGF2 alpha. PGF2 alpha stimulate the secretion of the luteal oxytocin **(Schall- enberger and Prokopp, 1984)** and oxytocin can increase production of PGFM (a metabolite of PGF2 alpha) and lead to earlier luteolysis **(Newcomp et al., 1977; Milvae and Hansel, 1980; Oyedipe et al., 1984; Troxel and Kesler, 1984; Larfance and Goff, 1985).**

Results of the current study agree with those obtained by **Cameron and Fosgate (1964); Short et al. (1972); and Stewart and Stevenson (1987).** The later author reported that frequent daily administration of (100 iu) oxytocin for 28 day postpartum failed to affect interval from parturition to ovulation and estrus. Similar results were obtained with use of 150 or 200 iu units one dose per day **(Cameron and Fosgate, 1964)** and 40 iu thrice daily **(Short et al., 1972)** who reported that treatment with oxytocin did not significantly hasten involution of the uterus.

In the present work, we did not examine the genital tract rectaly to evaluate uterine involution after administration of oxytocin. However, fertility parameters particularly number of services per conception is considered an indicator for uterine involution. We postulated that, treatment with oxytocin in the present study did not significantly hasten involution of the uterus.

Contrary to our results, **Mollo et al. (1997)** reported that oxytocin administration immediately after delivery able to reduce occurrence of retained fetal membranes in