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Effects of feeding OmniGen-AF® on superovulatory response in donor beef cows: I. Serum progesterone and cortisol, embryo recovery and quality

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ABSTRACT

Optimal results in cattle embryo transfer are limited by the variation in ova recovery, fertilization rate and embryo quality experienced with superovulation. Inflammation and immune dysregulation may be contributing factors. This study, evaluated feeding OmniGen-AF® (OG), a nutritional supplement that reduces inflammation and supports immune health, on superovulatory response and serum progesterone and cortisol concentrations in embryo donors treated with two different doses of Folltropin®-V (FSH). Angus cross-bred beef cows ($n = 24$) were assigned to four groups, fed OG at 0 or 56 g/animal/day for 49 days and were treated with 200 or 400 mg FSH to induce superovulation. Treatments for superovulation started after feeding OG for 28 days and ova were non-surgically recovered 7 days after estrus and graded for quality. More transferrable embryos ($P < 0.05$) were recovered from cows fed 56 g OG and treated with 400 compared with 200 mg FSH. Percent degenerate embryos recovered from cows treated with the 400 mg FSH dose was threefold greater ($P < 0.05$) when fed no OG compared with 56 g OG. Serum progesterone on day of embryo collection was greater ($P < 0.05$) in OG-supplemented cows and cows treated with 200 mg FSH. Serum cortisol was not affected ($P > 0.10$) by FSH dose or OG-feeding, but was greatest ($P < 0.05$) on Days 0 and 42 of the feeding period. In summary, the improvement in embryo quality with OG-feeding may relate to a greater serum progesterone concentration.

1. Introduction

Embryo transfer is an applied reproductive technology commonly used to improve female reproductive efficiency, herd genetics and propagate offspring from elite sire-dam matings (Bó and Mapletoft, 2014). Embryo collection is an important part of the embryo transfer procedure, as this procedure encompasses superovulation and breeding of the donor cow. Most superovulation protocols require donors to be confined to conduct the procedures related to the protocol as many as to two times each day for a week, which includes a 4-day regimen of twice-daily i.m. FSH injections [*e.g.,* Folltropin®-V (Bioniche, Athens, GA)] with an estrous synchronization protocol and 1 or 2 days of artificial insemination also being imposed (Bó and Mapletoft, 2014). Confining and administrations of treatments may cause an acute stress response in the donor. Stress has been associated with a reduced superovulation response and embryo quality (Edwards et al., 1987; Ealy et al., 1993; Macedo et al., 2011). During a stressful event, the hypothalamus releases

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corticotropin releasing hormone (CRH) which causes release of adrenocorticotropic releasing hormone (ACTH) from the pituitary gland. The target organ for ACTH is the adrenal cortex where there is regulation of cortisol release by ACTH causing several downstream negative physiologic effects on various organs. Reproductive performance suppression during stress is due to the negative feedback of cortisol on the hypothalamic-pituitary axis resulting in a decrease in luteinizing hormone (LH) pulse frequency. A decrease in LH pulse frequency suppresses follicular growth, ovulation rate, and fertilization (Dobson and Smith, 2000). Confinement and stress due to treatments, in the form of human-animal interactions, can have marked effects on viability of recovered embryos. Macedo et al. (2011) observed a 19% reduction in percent viable embryos recovered because of confinement and treatment of donors in ways that results in stress compared with unstressed control animals. Stress that results from stockpersons being loud in their vocalizations and extended times of confinement resulted in greater plasma cortisol in donor cows. Donor age and amount of nutritional intake are also factors affecting superovulation results (Kafi and McGowan, 1997).

One potential way to reduce the stress response during superovulation may be through feeding a nutritional supplement such as OmniGen-AF® (OG; Phibro Animal Health Corporation; Teaneck, NJ). Implementing nutritional strategies during the period a superovulation protocol is being imposed to improve embryo recovery and quality are not new approaches. Dietary adjustments in protein, fatty acids, vitamins and minerals to generate positive effects on superovulatory response have been evaluated (Velazquez, 2011). The OG dietary supplementation is a propriety blend of ingredients that when fed enhances overall animal health by reducing the inflammation response and supports immune health (Wang et al., 2009; Ryman et al., 2013) and thus represents a novel approach for nutritional supplementations during a period when superovulation protocols are being imposed. Supplementation with OG reduced several negative physiological responses to stressors, including responses to heat stress and pathogen challenge (Carroll and Forsberg, 2007; Rowson et al., 2011; Fabris et al., 2017).

In numerous studies, there has been investigation of the effects of FSH dose on response to superovulatory treatments (Lerner et al., 1986; Gonzalez et al., 1990; Barati et al., 2006). Ovulation rate increases as dose of FSH increases to a dose where ovulation rate eventually plateaus (Bó and Mapletoft, 2014). With respect to fertilization rate and transferrable embryo quality, the consensus is there are no detrimental effects when there are larger doses of FSH even for doses two-fold the recommended amount (Bó and Mapletoft, 2014). A repetitive ovarian stimulation with FSH on the same cow has negative effects on the recovery rate of embryos at day 7 of development (Lubbadeh et al., 1980). In the present study, there was an assessment of whether feeding OG would result in an interaction with FSH dose and repeated superovulation on transferrable embryo yield. The objective of this research, therefore, was to evaluate superovulatory responses and serum progesterone and cortisol concentrations in donor beef cows supplemented with OG and treated with 200 or 400 mg of FSH.

2. Materials and methods

2.1. Animal care and use

All animals were humanely treated and cared for in compliance with an approved protocol in accordance with Oregon State University IACUC Guidelines.

2.2. Animal housing and feeding

Cross-bred Angus cows (n = 24) were housed in a free stall barn at the Oregon State University Beef Center in Corvallis, OR with grass hay and water provide *ad libitum*. All cows individually received a mixture of ground corn and molasses mix one time each day. Cows were randomly sorted into four groups: supplementation with no or 56 g/OG/animal/day (completely mixed into the molasses and ground corn mixture) and treatment with 200 or 400 mg Folltropin V for the superovulatory treatment. Duration of OG feeding was 49 d with 28 d as a pre-feeding phase prior to the start of superovulation with six cows per treatment.

2.3. Estrous synchronization, superovulation and artificial insemination

In all cows, there was initiation of the estrous synchronization treatment regimen on Day 28 of the pre-feeding phase with a single injection IM of prostaglandin $F_{2\alpha}$ (PGF; Lutalyse®, Zoetis, Florham Park, NJ; Fig. 1). At 10 days after the first PGF injection there was initiation of the 4-day FSH treatment regimen. Cows treated for superovulation with 200 or 400 mg FSH received eight 25-mg doses or eight 50-mg doses two times each day, respectively. There was observation of all cattle for symptoms of behavioral estrus 24 h after last PGF injection with the majority of cows expressing estrus 36 h after the PG injection in all groups. Cows were artificially

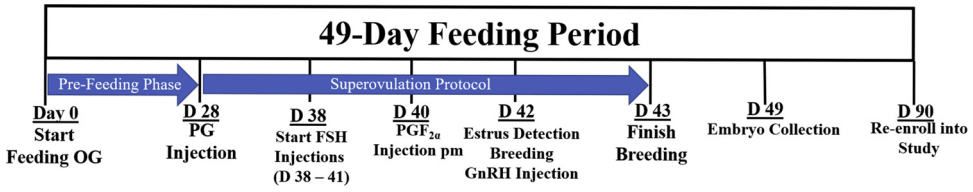

Fig. 1. Experiential timeline for the feeding and superovulation protocol.

inseminated with one 0.5-ml straw of semen at 0, 12, and 24 h after onset of behavioral estrus. Cows, not expressing behavioral estrus by 36 h after the last PGF injection, were subsequently artificially inseminated at 48, 60 and 72 h after this injection. All cows were administered 100 μg GnRH i.m. (Factrel®, Zoetis, Florham Park, NJ) at the time of the first artificial insemination (Fig. 1).

2.4. Serum collection and analysis

Blood samples were collected using jugular venipuncture on Days 0, 10, 14, 21, 28, 38, 40, 42, 43, and 49 of the study. Samples were collected in 10-ml serum separator tubes containing a clot activator and gel (BD Vacutainer systems, Franklin Lakes, NJ). Serum tubes were centrifuged at 3,000-×*g* for 20 min at 4 °C, sera were decanted and stored at −80 °C until further analysis.

Serum cortisol concentrations were determined using a commercially available EIA kit (Arbor Assays, Ann Arbor, MI) according to the manufacturer's instructions. Intra- and inter-assay coefficients of variation were 3.7% and 3.0%, respectively. There was quantification of serum progesterone concentrations using a commercially available ELISA kit (Enzo Life Sciences, Farmingdale, NY) following the manufacturer's guidelines. Intra- and inter-assay coefficients of variation were 3.3% and 6.7%, respectively.

2.5. Embryo collection and grading

Ova were non-surgically collected 7 d after estrous onset. Flush medium consisted of Dulbecco's phosphate buffered saline containing an antibiotic/antimycotic solution (Sigma-Aldrich, St. Louis, MO) and 0.2% heat-treated bovine fetal calf serum (Sigma-Aldrich, St. Louis, MO). Recovered ova were evaluated for fertilization and embryos were scored for developmental stage and quality using the four-rank grading scheme (excellent, good, fair and poor) based on blastomere integrity as described by Lindner and Wright (Linder and Wright, 1983).

Cows were assigned to a second replicate of the study that included OG-feeding and superovulation 90–120 d after the first replicate of the study was completed. All procedures conducted during the second replicate of the study were identical as those in the first replicate of the study.

2.6. Statistical analysis

Analyses of variance (ANOVA) for 2 × 2 × 2 factorial design were used to detect differences due to treatments in the following: total numbers of ova, embryos, transferrable embryos, degenerate embryos and unfertilized ova (UFO) recovered. Furthermore, there was assessment of the percentage of embryos, transferrable embryos, degenerate embryos and UFO recovered of the total number of ova recovered as well as serum progesterone concentrations on the day of embryo collection. Sources of variation in the ANOVA were FSH (200 or 400 mg), OG (0 or 56 g/animal/day), superovulation responses in the initial and subsequent replicates of the study (Replicate 1 or 2) and the FSH X OG, FSH X Replicate, OG X Replicate and the FSH X OG X Replicate interactions. A repeated measures ANOVA for a 2 × 2 × 2 factorial design was used to evaluate differences in serum cortisol concentrations during the feeding period. Sources of variation in the ANOVA were FSH, OG, Replicate, days of blood collection (Day) and the interactions. If significant effects were observed with the ANOVA analysis, differences between means were evaluated using the Fisher's least significant differences procedures. All analyses were performed using the NCSS statistical software program (Number Cruncher Statistical System; 2007, Jerry Hintze, Kaysville, UT).

3. Results

Of the 24 cows in which superovulation treatments were imposed, ova were collected from 20 cows in each Replicate of the study. The four cows from which there were no ova collected differed between Replicates 1 and 2 of the study. There were no differences ($P > 0.10$) in mean numbers of ova recovered for cows in which superovulation treatments were imposed using 200 or 400 mg FSH (4.3 ± 1.6 compared with 8.2 ± 1.6, respectively) or fed no or 56 g OG (5.8 ± 1.6 compared with 6.7 ± 1.6, respectively). More ($P = 0.05$) ova were recovered from cows in which superovulation was imposed in Replicate 1 compared to Replicate 2 of the study (7.5 ± 0.8 compared with 5.0 ± 0.8, respectively). None of the interactions were significant factors affecting mean number of ova recovered (Fig. 2). The total ova variable included values for both fertilized and unfertilized ova, with scoring to determine early embryonic development and quality of embryos.

Likewise, the mean numbers of embryos recovered were not affected ($P > 0.10$) by amount of FSH dose (200 mg, 5.4 ± 1.7 compared with 400 mg, 7.7 ± 1.5), amount of OG fed (No OG, 6.5 ± 1.7 compared with 56 g, 6.6 ± 1.6), Replicate of the study (Replicate 1, 7.6 ± 0.9 compared with Replicate 2, 5.6 ± 0.9) or any of the interactions (Fig. 3A). Percentage of embryos recovered was also not affected ($P > 0.10$) by dose of FSH (200 mg, 84 ± 8% compared with 400 mg, 80 ± 7%), amount of OG fed (No OG, 87 ± 8% compared with 56 g, 77 ± 7%), Replicate (Replicate 1, 80 ± 5% compared with Replicate 2, 84 ± 5%) or any of the interactions (Fig. 3B).

Mean numbers of transferrable embryos recovered from cows were not affected ($P > 0.10$) by dose of FSH (200 mg, 4.3 ± 1.4 compared with 400 mg, 6.2 ± 1.3), amount of OG (No OG, 4.9 ± 1.4 compared with 56 g, 5.7 ± 1.3) or Replicate (Replicate 1, 6.0 ± 0.7 compared with Replicate 2, 4.6 ± 0.7). There, however, were more ($P < 0.05$) transferrable embryos recovered from cows fed 56 g OG that were treated with 400 mg FSH compared with cows treated with 200 mg FSH (Fig. 3C). None of the other interactions was a significant factor affecting number of transferrable embryos recovered. The main effects of FSH (200 mg, 68 ± 9% compared with 400 mg, 61 ± 8%), amount of OG fed (No OG, 63 ± 9% compared with 56 g, 65 ± 8%), Replicate (Replicate 1,

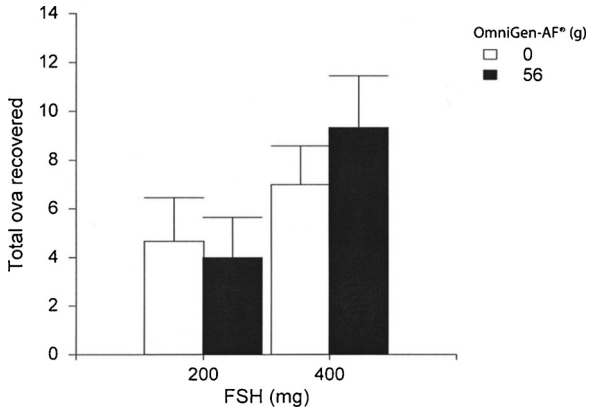

Fig. 2. Number of ova (mean ± SE) recovered from cows (n = 24) treated with 200 or 400 mg FSH as a superovulation treatment and not fed or fed 56 g OmniGen-AF®.

63 ± 5% compared with Replicate 2, 66 ± 5%) and the interactions did not affect ($P >$ 0.10) percentage of transferrable embryos recovered (Fig. 3D).

Numbers of degenerate embryos recovered from cows did not differ ($P >$ 0.10) when there was treatment with FSH (200 mg, 1.1 ± 0.4 compared with 400 mg, 1.5 ± 0.4) or Replicate (Replicate 1, 1.6 ± 0.3 compared with Replicate 2, 1.0 ± 0.3) or any of the interactions (Fig. 4A). There, however, were more ($P =$ 0.09) degenerate embryos recovered from cows that were fed no OG compared with those fed 56 g OG (1.7 ± 0.4 compared with 0.9 ± 0.4, respectively). Percentage of degenerate embryos recovered was also not affected ($P >$ 0.10) by FSH dose (200 mg, 16 ± 5% compared with 400 mg, 20 ± 4%) or Replicate (Replicate 1, 17 ± 5% compared with Replicate 2, 19 ± 5%). Percentage of degenerate embryos recovered was greater ($P =$ 0.07) from cows not fed OG compared with those fed 56 g OG (No OG, 24 ± 5% compared with 56 g, 12 ± 5%) and the FSH X OG interaction was significant. When there was treatment with 400 mg FSH, percent degenerate embryos recovered was greater ($P <$ 0.05) in cows that were not fed OG compared with those fed 56 g OG (Fig. 4B).

There were no differences ($P >$ 0.10) in unfertilized ova (UFO) recovered for cows treated with 200 or 400 mg FSH (0.8 ± 0.3 compared with 1.1 ± 0.3), not fed OG or those that were fed 56 g OG (0.7 ± 0.3 compared with 1.2 ± 0.3, respectively) and between Replicates 1 and 2 of the study (1.2 ± 0.3 compared with 0.7 ± 0.3, respectively). None of the interactions were significant factors affecting mean numbers of UFO recovered (Fig. 4C). Percentages of UFO recovered were not affected ($P >$ 0.10) by dose of FSH (200 mg, 16 ± 8% compared with 400 mg, 19 ± 7%), amount of OG fed (No OG, 12 ± 8% compared with 56 g, 23 ± 7%), Replicate (Replicate 1, 20 ± 5% compared with Replicate 2, 15 ± 5%) or any of the interactions (Fig. 4D).

Serum progesterone concentrations on Day 7 differed ($P <$ 0.05) as a result of FSH dose (200 mg, 14.7 ± 1.9 compared with 400 mg, 9.1 ± 1.9 ng/ml) and amount of OG fed (No OG, 8.8 ± 1.9 compared with 56 g, 15.0 ± 1.9 ng/ml) and the FSH X OG interaction was significant. Serum progesterone concentration was greater ($P <$ 0.05) in cows fed 56 g OG and treated with 200 mg FSH compared with cows treated with 400 mg FSH or those not fed OG and treated with either dose of FSH (Fig. 5). Replicate of the study (Replicate 1, 12.7 ± 2.0 compared with Replicate 2, 11.1 ± 2.2 ng/ml) and the other interactions were not significant factors affecting serum progesterone concentrations.

Serum cortisol concentrations did not differ ($P >$ 0.10) as a result of FSH dose (200 mg, 226.6 ± 24.3 compared with 400 mg, 241.7 ± 24.4 pg/ml) or amount of OG fed (No OG, 243.9 ± 24.3 compared with 56 g, 224.4 ± 24.4 pg/ml) but were less ($P <$ 0.05) in Replicate 1 compared with Replicate 2 of the study (213.0 ± 10.9 compared with 255.3 ± 11.1 pg/ml). Cortisol concentrations also differed ($P <$ 0.05) by Day where there was the least concentration at the end of the feeding period, Day 49, and greater concentrations at the start of the feeding period, Day 0, and at onset of estrus and the day of the first insemination, Day 42 (Table 1). The FSH X Round interaction was also a factor contributing to differences in serum cortisol concentrations. Serum cortisol was greater ($P <$ 0.05) in cows treated with 400 compared with 200 mg FSH in Replicate 2 and cows treated with both doses of FSH in Replicate 1 of the study (Fig. 6). The remaining interactions were not significant factors affecting serum cortisol concentrations.

4. Discussion

Ova and embryo recoveries were greater in the first compared to the second replicate of the superovulation regimen in the present study. These results are consistent with results in previous studies where donor cows naive to a adapting to the superovulation treatment regimen had greater ova recovery rates compared to when there were subsequent treatments of the same cows for superovulation (Lubbadeh et al., 1980). Although the results are inconsistent with respect to the effects of season, this factor may also have exerted an effect on ova recovery because Replicates 1 and 2 of the present study were conducted during December to April and April to August, respectively (Kafi and McGowan, 1997). The effects of heat stress on embryo production and recovery are well documented, however, replicate of the study was not a significant factor in affecting the number of transferrable and degenerate embryos or UFO recovered in the present study. Thus, the effects of relatively greater ambient temperatures during a period where a

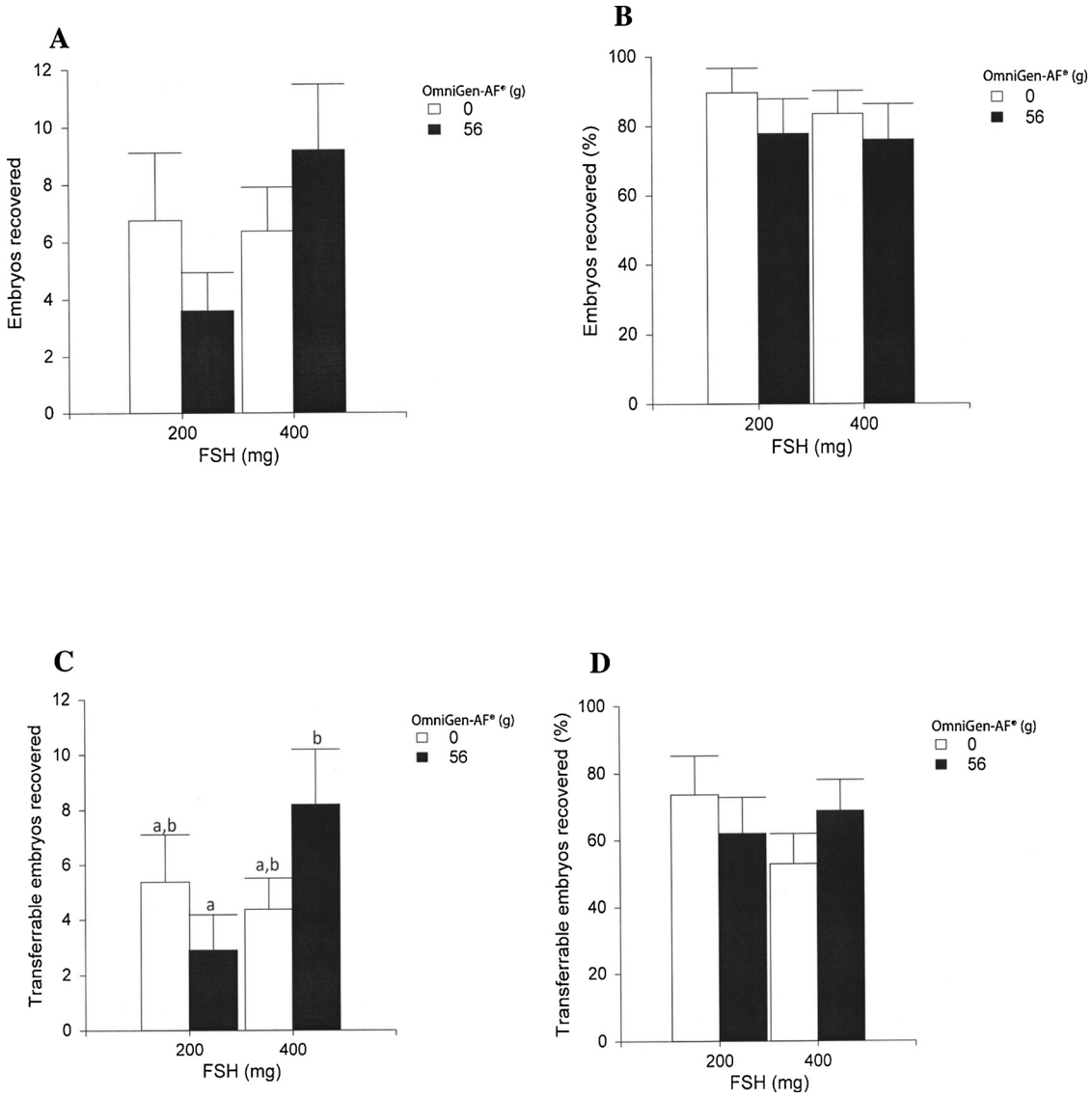

Fig. 3. Embryo recovery data from cows (n = 20) treated with 200 or 400 mg FSH as a superovulation treatment and not fed or fed 56 g OmniGen-AF®.

A. Total embryos (mean ± SE) recovered from cows (n = 20) treated with 200 or 400 mg FSH and not fed or fed 56 g OmniGen-AF®.

B. Percent embryos (mean ± SE) recovered from cows treated with 200 or 400 mg FSH and not fed or fed 56 g OmniGen-AF®.

C. Transferrable embryos (mean ± SE) recovered from cows treated with 200 or 400 mg FSH and not fed or fed 56 g OmniGen-AF®.

[a,b]Means without similar superscripts differ ($P < 0.05$).

D. Percent transferrable embryos (mean ± SE) recovered from cows treated with 200 or 400 mg FSH and not fed or fed 56 g OmniGen-AF®.

superovulation regimen was imposed in the current study was negligible (Kafi and McGowan, 1997).

Ova and embryo recoveries were not affected by OG feeding or FSH dose in the present study. Donor cows fed OG had more transferrable embryos, however, when there was treatment with 400 mg FSH and fewer embryos were degenerate in the group administered this FSH dose. The effects of diet on embryo development can be far reaching. Wrenzycki et al. (2000) reported there were changes in sodium/potassium ATPase and Cu/Zn superoxide dismutase gene expression in cattle embryos due to donor cow diet. Both enzymes are important for early embryo development, especially the sodium/potassium ATPase that has an important function in blastocoel formation. The approach in the present study was to utilize a different nutritional strategy by incorporating a supplement to the diet that the cattle had previously been fed. Embryo transcription processes in cattle were also altered when dams were supplemented with methionine (Peñagaricano et al., 2013). How OG functions to improve embryo quality is not clear but it is known OG reduces inflammation and the negative physiologic responses to heat stress and pathogen challenge (Carroll and Forsberg, 2007; Rowson et al., 2011; Fabris et al., 2017). With ovulation being considered to induce an inflammatory response, OG may induce some reduction of inflammation during superovulation (Espey, 1980). Exogenous FSH treatments are believed to inhibit the

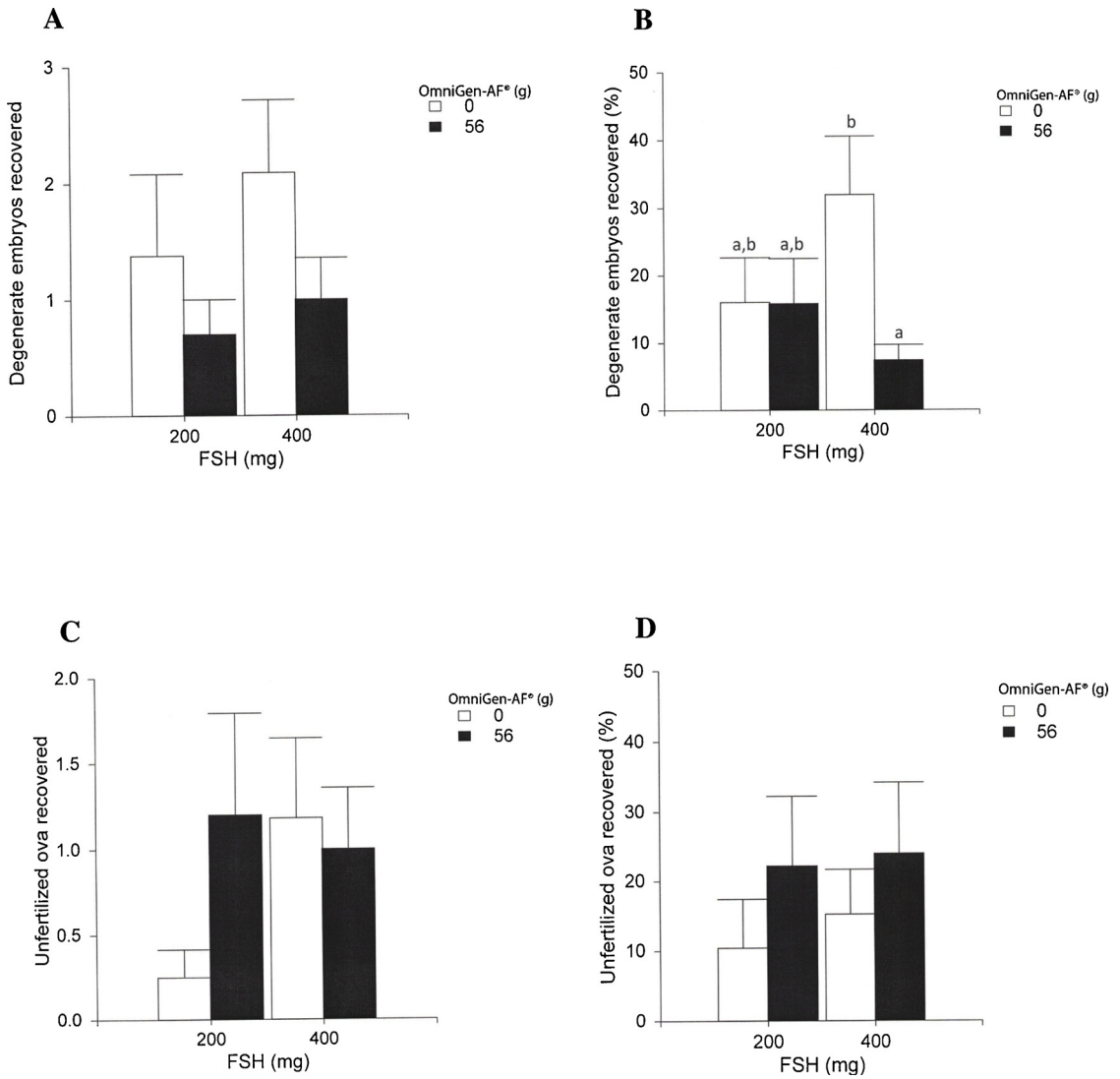

Fig. 4. Degenerate embryo and unfertilized ova data from cows treated with 200 or 400 mg FSH as a superovulation treatment and not fed or fed 56 g OmniGen-AF®.

A. Degenerate embryos (mean ± SE) recovered from cows treated with 200 or 400 mg FSH and not fed or fed 56 g OmniGen-AF®.

B. Percent degenerate embryos (mean ± SE) recovered from cows treated with 200 or 400 mg FSH and not fed or fed 56 g OmniGen-AF®.

[a,b]Means without similar superscripts differ ($P < 0.05$).

C. Unfertilized ova (mean ± SE) recovered from cows treated with 200 or 400 mg FSH and not fed or fed 56 g OmniGen-AF®.

D. Percent unfertilized ova (mean ± SE) recovered from cows treated with 200 or 400 mg FSH and not fed or fed 56 g OmniGen-AF®.

regression of follicles destined to undergo atresia and some of these follicles may have suboptimal oocyte development leading to early embryonic developmental abnormalities and ultimately development of non-viable embryos (Monniaux et al., 1983; King et al., 1987). Feeding OG to cattle during the period when the superovulation protocol was imposed may sustain the viability of follicles and oocytes contained within follicles that were progressing toward atresia. The OG may also function indirectly to induce an antioxidant effect at the ovary similar to the manner in which antioxidants ameliorate the effects of stress on oocyte quality. Oocyte quality is less during periods of ambient heat and restraint stress because mitochondrial gene expression associated with oxidative phosphorylation is impaired thereby reducing ATP production and compromising oocyte maturation and early embryonic development (Roth, 2018). Stress also decreases glutathione production, resulting in reactive oxygen species to exert deleterious effects on embryo survival. For example, Lian et al. (2013) injected epigallocatechin-gallate, the green tea flavonoid antioxidant, into restraint-stressed mice during the period of oocyte maturation and improved early embryo development and blastocyst formation by decreasing the induced oxidative stress response.

Serum progesterone concentrations on Day 7 at the time of embryo collection were greater in cows treated with 200 compared with 400 mg FSH and fed 56 g compared with no OG, with the greatest progesterone concentration in cows treated with 200 mg FSH

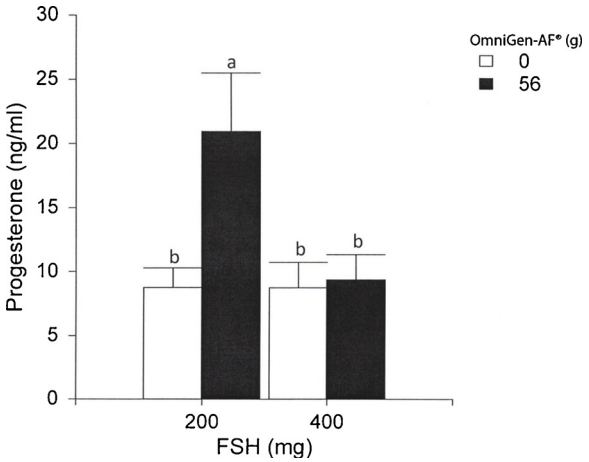

Fig. 5. Serum progesterone concentrations (ng/ml) at time of embryo collection in donor beef cows fed OmniGen-AF® during superovulation with FSH; [a,b]Means without similar superscripts differ ($P < 0.05$).

Table 1
Serum cortisol concentrations (pg/ml) pooled for the two replicates of the study in donor beef cows during OmniGen-AF® feeding and treatments with FSH for superovulation.

Day	Cortisol (pg/ml)[a]
0	397.0 ± 24.3[b]
10	194.2 ± 24.3[c,d,e]
14	224.1 ± 24.3[c,d]
21	170.6 ± 24.3[d,e]
28	192.8 ± 24.3[c,d,e]
38	245.4 ± 24.3[c]
40	244.2 ± 25.7[c]
42	330.4 ± 24.3[b]
43	207.8 ± 24.3[c,d]
49	135.2 ± 26.0[e]

[a]Values reported are means ± SE.
[b,c,d,e]Means without similar superscripts differ ($P < 0.05$).

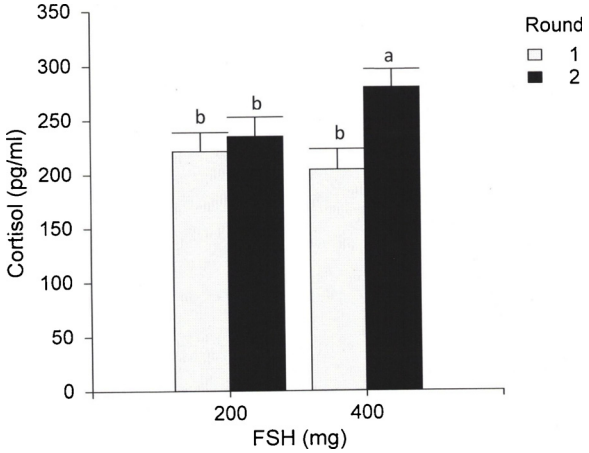

Fig. 6. Serum cortisol concentrations (pg/ml) in donor beef cows during OmniGen-AF® feeding and during the period of treatments for superovulation with FSH between Replicates 1 and 2 of study; [a,b]Means without similar superscripts differ ($P < 0.05$).

and fed 56 g OG. Ova recovery data indicate there was no difference in corpora lutea number among the four treatment groups leading to the conclusion corpora lutea in the 200 mg FSH/56 g OG group were more functional and produced more progesterone, possibly because these structures were larger (Lüttgenau et al., 2011). After ovulation, there is an increase in the number of ovarian innate immune cells, such as macrophages, lymphocytes and neutrophils, to clear the ovulation site of degenerating cells and tissue debris resulting from ovulation and in the transformation of granulosa and theca interna cells into large and small luteal cells (Turner et al., 2012). The OG feeding has a beneficial effect in supporting the innate immune system during an inflammatory response (Rowson et al., 2011). The potential benefit of feeding OG to donor cows may be related to augmenting the innate immune system for remodeling the ovulation sites thereby promoting development of more functional corpora lutea. Circulating progesterone concentration during this time is important for early embryo development because of the temporal and cell-specific changes occurring in the uterus to support development (Forde et al., 2015).

Serum cortisol concentrations were quantified throughout the feeding period and were affected only by Replicate of study and Day of blood collection. Serum cortisol was less for cows in Replicate 1 compared with Replicate 2 of the study and there was a FSH x Replicate interaction in which cows treated with 400 mg FSH in Replicate 2 of the study had the greatest cortisol concentration. The interaction with FSH dose is difficult to explain, however, the greater cortisol concentration in Replicate 2 of the study may represent a heightened response to the confinement conditions and treatment procedures that these cows previously experienced in Replicate 1. Serum cortisol concentrations were greatest on Days 0 and 42 and least on Day 49, the day of embryo collection and the last day of feeding. Relatively greater cortisol concentrations on Day 0, the start of the study, is not unexpected because this was the first time with these cows where there was an imposing of the confinement and treatment procedures required for blood collection, including movement and restraint for jugular blood withdrawal. Cortisol concentrations decreased as the study continued likely due to acclimation to the handling procedures but increased on Day 42 during estrus. Cows in behavioral estrus are more physically active and there are other associated changes which leads to an increase in serum cortisol (Lyimo et al., 2000).

5. Conclusion

Results from the present study indicate feeding OG increases transferrable embryo yield and reduces degenerate embryo recovery from cows treated with 400 mg FSH for superovulation. There, however, is no increase in progesterone at this time point, which warrants future research to investigate mechanisms regulating improved embryo yield. Feeding of OG was also associated with greater progesterone concentrations at the time of embryo collection in cows treated with 200 mg FSH, which may be indicative of luteal functions during this period of early embryonic development. There needs to be research conducted to elucidate the mechanisms supporting the changes in embryo quality and progesterone concentrations observed during OG feeding in the present study. Overall, the results support the thought that there is a beneficial effect on improving transferrable embryo production when donor cows are fed OG during the period when superovulation procedures are being imposed.

Declaration of Competing Interest

D. McLean is an employee of Phibro Animal Health Corporation. The authors have no conflict of interests regarding publication of this manuscript.

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References

Barati, F., Niasari-Naslaji, A., Bolourchi, M., Sarhaddi, F., Razavi, K., Naghzali, E., Thatcher, W.W., 2006. Superovulatory response of Sistani cattle to three different doses of FSH during winter and summer. Theriogenology 66, 1149–1155.
Bó, G.A., Mapletoft, R.J., 2014. Historical perspectives and recent research on superovulation in cattle. Theriogenology 81, 38–48.
Carroll, J.A., Forsberg, N.E., 2007. Influence of stress and nutrition on cattle immunity. Vet. Clin. North Am. Food Anim. Pract. 23, 105–149.
Dobson, H., Smith, R., 2000. What is stress, and how does it affect reproduction? Anim. Reprod. Sci. 60, 743–752.
Ealy, A.D., Drost, M., Hansen, P.J., 1993. Developmental changes in embryonic resistance to adverse effects of maternal heat stress in cows. J. Dairy Sci. 76, 2899–2905.
Edwards, L.M., Rache, C.H., Griffin, J.L., Wolfe, D.F., Marple, D.N., Cummins, K.A., Pitchett, J.F., 1987. Effect of transportation stress on ovarian function in superovulated Hereford heifers. Theriogenology 28, 291–299.
Espey, L.L., 1980. Ovulation as an inflammatory reaction—A hypothesis. Biol. Reprod. 22, 73–106.
Fabris, T.F., Laporta, J., Corra, F.N., Torres, Y.M., Kirk, D.J., McLean, D.J., Chapman, J.D., Dahl, G.E., 2017. Effect of nutritional immunomodulation and heat stress during the dry period on subsequent performance of cows. J. Dairy Sci. 100, 6733–6742.
Forde, N., Bazer, F.W., Spencer, T.E., Lonergan, P., 2015. "Conceptualizing" the endometrium: identification of conceptus-derived proteins during early pregnancy in cattle. Biol. Reprod. 92 156–156.
Gonzalez, A., Lussier, I.G., Carruthers, T.D., Murphy, B.D., Mapletoft, R.J., 1990. Superovulation of beef heifers with Folltropin: a new FSH preparation containing reduced LH activity. Theriogenology 33, 519–529.
Kafi, M., Mcgowan, M.R., 1997. Factors associated with variation in the superovulatory response of cattle. Anim. Reprod. Sci. 48, 137–157.
King, W.A., Guay, P., Picard, L., 1987. A cytogenetical study of 7-day-old bovine embryos of poor morphological quality. Genome 29, 160–164.
Lerner, S., Thyane, W.V., Baker, R.D., Henschen, T., Meredith, S., 1986. Age, dose of FSH and other factors affecting superovulation in Holstein cows. J. Anim. Sci. 63, 176–183.
Lian, H.-Y., Gao, Y., Jiao, G.-Z., Sun, M.-J., Wu, X.-F., Wang, T.-Y., Li, H., Tan, J.-H., 2013. Antioxidant supplementation overcomes the deleterious effects of maternal restraint stress-induced oxidative stress on mouse oocytes. Reproduction 146, 559–568.

Linder, G.M., Wright, R.W., 1983. Bovine embryo morphology and evaluation. Theriogenology 20, 407–416.
Lubbadeh, W.F., Graves, C.N., Spahr, S.L., 1980. Effect of repeated superovulation on ovulatory response of dairy cows. J. Anim. Sci. 50, 124–127.
Lüttgenau, J., Ulbrich, S.E., Beindorff, N., Honnens, A., Herzog, K., Bollwein, H., 2011. Plasma progesterone concentrations in the mid-luteal phase are dependent on luteal size, but independent of luteal blood flow and gene expression in lactating dairy cows. Anim. Reprod. Sci. 125, 20–29.
Lyimo, Z.C., Nielen, M., Ouweltjes, W., Kruip, T.A., van Eerdenburg, F.J., 2000. Relationship among estradiol, cortisol and intensity of estrous behavior in dairy cattle. Theriogenology 53, 1783–1795.
Macedo, G.G., Estefânia Serra Neto Zúccari, C., Gomes Pinto de Abreu, U., Alberto Negrão, J., Vianna da Costa Silva, E., 2011. Human–animal interaction, stress, and embryo production in Bos indicus embryo donors under tropical conditions. Trop. Anim. Health Prod. 43, 1175–1182.
Monniaux, D., Chupin, D., Saumande, J., 1983. Superovulatory responses of cattle. Theriogenology 19, 55–81.
Peñagaricano, F., Souza, A.H., Carvalho, P.D., Driver, A.M., Gambra, R., Kropp, J., Hackbart, K.S., Luchini, D., Shaver, R.D., Wiltbank, M.C., Khatib, H., 2013. Effect of maternal methionine supplementation on the transcriptome of bovine preimplantation embryos. PLoS One 8, e72302.
Roth, Z., 2018. Symposium review: reduction in oocyte developmental competence by stress is associated with alterations in mitochondrial function. J. Dairy Sci. 101, 3642–3654.
Rowson, A.D., Wang, Y.-Q., Aalseth, E., Forsberg, N.E., Puntenney, S.B., 2011. Effects of an immunomodulatory feed additive on the development of mastitis in a mouse infection model using four bovine-origin isolates. Animal 5, 220–229.
Ryman, V.E., Nickerson, S.C., Kautz, F.M., Hurley, D.J., Ely, L.O., Wang, Y.Q., Forsberg, N.E., 2013. Effect of dietary supplementation on the antimicrobial activity of blood leukocytes isolated from Holstein heifers. Res. Vet. Sci. 95, 969–974.
Turner, M.L., Healey, G.D., Sheldon, I.M., 2012. Immunity and inflammation in the uterus. Reprod. Domest. Anim. 47, 402–409.
Velazquez, M.A., 2011. The role of nutritional supplementation on the outcome of superovulation in cattle. Anim. Reprod. Sci. 126, 1–10.
Wang, Y.Q., Puntenney, S.B., Burton, J.L., Forsberg, N.E., 2009. Use of gene profiling to evaluate the effects of a feed additive on immune function in periparturient dairy cattle. J. Anim. Physiol. Anim. Nutr. (Berl.) 93, 66–75.
Wrenzycki, C., De Sousa, P., Overström, E.W., Duby, R.T., Herrmann, D., Watson, A.J., Niemann, H., O'Callaghan, D., Boland, M.P., 2000. Effects of superovulated heifer diet type and quantity on relative mRNA abundances and pyruvate metabolism in recovered embryos. J. Reprod. Fertil. 118, 69–78.