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Final Scientific Report

Cover Page

BARD Project Number: US-3422-03 R

Date of Submission of the report: April 30, 2007

Project Title:

Investigators

Institutions

Principal Investigator (PI): W.R. Butler

Cornell University
Agriculture Research

Co-Principal Investigator (Co-PI): U. Moallem

Organization, Volcani Ctr

Collaborating Investigators: R.O. Gilbert

Cornell University

D. Sklan/A. Arieli

Hebrew University

Keywords *not* appearing in the title and in order of importance. Avoid abbreviations.

Abbreviations commonly used in the report, in alphabetical order:

Budget: IS: \$155,000

US: \$155,000

Total: \$310,000

W.R. Butler

Signature
Principal Investigator

Christina M. Abbott

Signature
Authorizing Official, Principal Institution

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Cover Page - Scientific Report

BARD Project Number: US-3422-03 RTitle: Prepartum Dietary Supplementation to Enhance Fertility in High Yielding Dairy Cows

Investigators:

Affiliated Institutions:

W.R. ButlerCornell UniversityR.O. GilbertCornell UniversityU. MoallemAgriculture Research Organization Volcani CtrD. Sklan/A. ArieliHebrew UniversityStart Date of Project: September 1, 2003

Date of Submission of Report: April 30, 2007

First Annual Report: August 30, 2004Second Annual Report: September 7, 2005Third Annual Report: August 30, 2006Signature
Principal Investigator (PI)Signature
Institution's Authorizing Official, Principal Institution

31-12-2007

Final Scientific Report

Publication Summary (numbers)

	Joint IS/US authorship	US Authors only	Israeli Authors only	Total
Refereed (published, in press, accepted) BARD support acknowledged			2	2
Submitted, in review, in preparation		1		1
Invited review papers				
Book chapters				
Books				
Master theses			1	1
Ph.D. theses		1	1	2
Abstracts			2	2
Not refereed (proceedings, reports, etc.)				

Postdoctoral Training: List the names and social security/identity numbers of all postdocs who received more than 50% of their funding by the grant.

Cooperation Summary (numbers)

	From US to Israel	From Israel to US	Together, elsewhere	* Total
Short Visits & Meetings		1		1
Longer Visits (Sabbaticals)				

Description Cooperation:

This project combined the expertise of Dr. Butler for hormone relationships underlying ovarian follicular and uterine functions and Dr. Moallem for analysis of follicle fluids in high yielding dairy cows. Similar dietary formulations and dietary supplements (fats and propylene glycol) were fed in both countries to advance understanding of the interaction between liver function and reproductive performance under different management systems. Dr. Moallem traveled to Cornell University in May 2006. The data collected from the project during the first two years from both countries was discussed for important understanding of the effects of dietary supplements and new directions toward completion of the project objectives and submission of publications.

Patent Summary (numbers)

	Israeli inventor only	US inventor only	Joint IS/US inventors	Total
Submitted				
Issued (allowed)				
Licensed				

Abstract

Objectives of the project:

1. To evaluate the effects of a glucogenic supplement during the peripartum transition period on insulin, hepatic triglyceride accumulation, interval to first ovulation, and progesterone profile in dairy cows.
2. To compare benefits of supplemental fats differing in fatty acid composition and fed prepartum on hepatic triglyceride accumulation, interval to first ovulation, progesterone profile, and uterine prostaglandin production in lactating dairy cows.
3. To assess the differential and carry-over effects of glucogenic and fat supplements fed to peripartum dairy cows on steroidogenesis and fatty acids in ovarian follicles.
4. To determine the carry-over effects of peripartum glucogenic or fat supplements on fertility in high producing dairy cows (modified in year 3 to Israel only).
5. Added during year 3 of project: To assess the activity of genes related to hepatic lipid oxidation and gluconeogenesis following dietary supplementation (USA only).

Background: High milk yields in dairy cattle are generally associated with poor reproductive performance. Low fertility results from negative energy balance (NEBAL) of early lactation that delays resumption of ovarian cycles and exerts other carryover effects. During NEBAL, ovulation of ovarian follicles is compromised by low availability of insulin and insulin-like growth factor-I (IGF-I), but fatty acid mobilization from body stores is augmented. Liver function during NEBAL is linked to the resumption of ovulation and fertility: 1) Accumulation of fatty acids by the liver and ketone production are associated with delayed first ovulation; 2) The liver is the main source of IGF-I. NEBAL will continue as a consequence of high milk yield, but dietary supplements are currently available to circumvent the effects on liver function.

For this project, supplementation was begun prepartum prior to NEBAL in an effort to reduce detrimental effects on liver and ovarian function. Fats either high or low in unsaturated fatty acids were compared for their ability to reduce liver triglyceride accumulation. Secondly, feeding specific fats during a period of high lipid turnover caused by NEBAL provides a novel approach for manipulating phospholipid pools in tissues including ovary and uterus. Increased insulin from propylene glycol (glucogenic) was anticipated to reduce lipolysis and increase IGF-I. The same supplements were utilized in both the USA and Israel, to compare effects across different diets and environments.

Conclusions: High milk production and very good postpartum health was achieved by dietary supplementation. Peripartum PGLY supplementation had no significant effects on reproductive variables. Prepartum fat supplementation either did not improve metabolic profile and ovarian and uterine responses in early lactation (USA) or decreased intake when added to dry cow diets (Israel). Steroid production in ovarian follicles was greater in lactating dairy cows receiving supplemental fat (unsaturated), although in a field trial fertility to insemination was not improved.

Implications: Supplemental dietary fat for dairy cows, especially unsaturated fatty acids, may be a useful strategy to achieve high milk production, while supporting ovarian responses that may benefit fertility during the breeding period.

Achievements

Objectives of the project:

1&2. To evaluate and compare the effects of feeding either a glucogenic supplement during the peripartum transition period or supplemental fats differing in fatty acid composition prepartum on insulin, hepatic triglyceride accumulation, first ovulation, progesterone profile, and uterine prostaglandin production in dairy cows.

In both countries milk production and feed intake did not differ in response to propylene glycol (PGLY) treatment and the metabolic status of cows was very similar. No significant differences were observed in plasma glucose, NEFA, insulin-like growth factor I (IGF-I), or β -hydroxybutyrate (BHB) concentrations compared to control cows. Hepatic triglyceride content did not differ from control during PGLY treatment. Ovarian follicular development, days to first ovulation, and cows ovulating by day 70 of lactation (~93%) were not significantly affected by PGLY treatment.

The metabolic response to feeding supplemental fats during the last three weeks before calving was different between cows in USA and Israel. In USA, milk production, feed intake, and net energy balance prepartum and postpartum were not different among treatment groups. Similarly, no significant differences were observed in plasma glucose, NEFA, insulin-like growth factor I (IGF-I) or hepatic triglyceride content, but the fat supplements tended to decrease β -hydroxybutyrate postpartum compared to control cows. Days to first ovulation and incidence of ovulation by day 70 of lactation were not significantly improved by fat supplementation. During the breeding period, uterine prostaglandin ($\text{PGF}_{2\alpha}$) production in response to an oxytocin challenge was not significantly different among treatments *ie.* no carry-over effect of prepartum fat supplementation. Overall, prepartum fat supplementation did not result in substantial improvement of metabolic profile in early lactation nor affect days to first ovulation and uterine prostaglandin response to an oxytocin challenge.

3. To assess the differential and carry-over effects of glucogenic and fat supplements fed to peripartum dairy cows on steroidogenesis and fatty acids in ovarian follicles. In Israel, prepartum dry matter intake was lower in cows supplemented with saturated fat (PrFA) and unsaturated fat (CaLFA) than in control and daily average calculated energy balance during the first 21 d in milk was lower. Consequently, plasma glucose and insulin concentrations pre and postpartum were lower, prepartum NEFA higher, and postpartum plasma β -hydroxybutyrate higher in the PrFA and CaLFA groups than in the control. Also differences between PrFA and CaLFA

groups were observed; dry matter intake was higher pre and postpartum in PrFA group than in CaLFA group and prepartum plasma NEFA concentrations were 19% higher and insulin concentrations were 21% lower in CaLFA group than in PrFA group.

The concentrations of androstenedione and estradiol in the follicular fluid of estradiol-active follicles on d 12 of lactation was higher in the group supplemented pre and postpartum with CaLFA than in all other groups. Follicular aspiration was repeated about 50 days later as fat supplementation continued. The results of improved steroidogenesis were strikingly similar with estradiol and androstenedione concentrations 40-70 % higher, higher estradiol to progesterone ratio, and larger follicular diameter in response to CaLFA.

Overall, feeding fat to cows during late pregnancy decreased the intake and negatively affected the metabolic status of the cows as reflected by plasma metabolites. However, continuing CaLFA supplementation during lactation improved the steroidogenic function of ovarian follicles, especially during the usual breeding period.

4. To determine the carry-over effects of fat supplements on fertility in high producing dairy cows (modified in year 3 to Israel only).

Overall, although we found in our previous study that cows that were supplemented with fat that contained high proportion of unsaturated FA showed greater steroidogenic activity in preovulatory follicles than in cows fed saturated FA, no increase was observed in fertility parameters in the current trial. Further field trials with other amounts of supplements are needed to determine the effects of unsaturated FA on fertility

5. Added during year 3 of project: To assess the activity of four genes related to hepatic lipid oxidation and gluconeogenesis following dietary supplementation (USA only).

Methodology (mRNA analysis) related to hepatic metabolism was successfully developed. On d 8 of lactation, abundance and expression of mRNA for gluconeogenic and lipid oxidation genes was not different among treatment groups indicating no carry-over effects of prepartum fat supplementation or response to ongoing propylene glycol treatment.

Conclusions and significance:

High milk production and very good postpartum health including hepatic metabolism was achieved by dietary supplementation. Peripartum PGLY supplementation had no significant effects on reproductive variables. Prepartum fat supplementation either did not improve metabolic profile and ovarian and uterine responses in early lactation (USA) or decreased intake when added

to dry cow diets (Israel). Steroid production in ovarian follicles was greater in lactating dairy cows receiving supplemental fat (unsaturated), although fertility to insemination was not improved.

Description of the cooperation:

This project took advantage of the combined expertise of Dr. Butler for metabolic relationships underlying follicle development and ovulation during NEBAL and Dr. Moallem for aspiration and analysis of follicle fluids in high yielding dairy cows. By applying very similar dietary formulations and the same dietary supplements (fats and propylene glycol) to peripartum cows in both countries, the research was directed toward the interaction between dietary feed intake and specific supplements on liver function, ovarian follicular steroidogenesis and reproductive performance under different management systems. In May 2006, Dr. Moallem traveled to Cornell University to meet with Dr. Butler. During the meeting, the data collected from the project during the first two years from both countries was reviewed and discussed yielding important understanding of the effects of dietary treatments and new directions toward completion of the project objectives and submission of publications. In addition, Dr. Moallem gave a presentation in the department of animal science of Cornell representing the results of the Israeli part of the project. In year three Dr. Moallem conducted a field trial in a large dairy herd based on the very interesting effects of dietary fatty acids on follicular fluid estradiol levels. Dr. Butler's lab contributed information on new molecular mRNA approaches for understanding the effects of the dietary fat supplements on liver function and metabolism (lipid oxidation and gluconeogenesis).

List of Publications:

Moallem, U., M. Katz, H. Lehrer, L. Livshitz, and S. Yakoby. Role of Peripartum Dietary Propylene Glycol or Protected Fats on Metabolism and Early Postpartum Ovarian Follicles. J. Dairy Sci. 90:1243–1254, 2007.

Moallem, U., M. Katz, A. Arieli, H. Lehrer. Effects of peripartum propylene glycol or fats differing in fatty acid profiles on feed intake, production and plasma metabolites in dairy cows. J. Dairy Sci. (Accepted).

Castañeda-Gutiérrez, E., S. H. Pelton, R. O. Gilbert, and W. R. Butler. Effect of Peripartum Dietary Supplementation of Dairy Cows on Metabolites, Liver Function and Reproductive Variables. Anim. Reprod. Sci. (submitted).

Appendix

Table of Contents

Published Papers

Moallem, U., M. Katz, H. Lehrer, L. Livshitz and S. Yakoby. 2007. Role of peripartum dietary propylene glycol or protected fats on metabolism and early postpartum ovarian follicles. J. Dairy Sci. 90:1243-1254.

In Press/Accepted or Submitted Papers

Moallem, U., M. Katz, A. Arieli and H. Lehrer. 2007. Effects of peripartum propylene glycol or fats differing in fatty acid profiles on feed intake, production and plasma metabolites in dairy cows. J. Dairy Sci. (Accepted).

Castaneda-Gutierrez, E., S.H. Pelton, R.O. Gilbert and W.R. Butler. 2007. Effect of peripartum dietary supplementation of dairy cows on metabolites, liver function and reproductive variables. ARS (Submitted).

Moallem, U. (et al.) 2007. Improved steroidogenesis of preovulatory follicle in dairy cows supplemented with fat containing high ratio of unsaturated fatty acids. (Unpublished data).

Moallem, U. (et al.) 2007. The effects of supplementing two dietary fats differing in saturation degree of fatty acids (Adolac or Megalac-R), from parturition until 100 DIM on milk production and fertility in high producing dairy cows. (Unpublished data).