Progesterone Based Synchrony Programmes in Dairy Cattle – Recent New Zealand Research

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Introduction

Under the NZ seasonal dairy system there is only a very short window of opportunity to ensure that relatively freshly calved cows have fertile reproductive cycles and get pregnant in time for the following calving period. It is important therefore that cows resume normal cycling activity closely following calving in order to maximize submission and conception rates in the following mating period.

Anoestrus in dairy cows has a significant impact on reducing submission rates. Various estimates of anoestrus in NZ dairy cattle about 10 years ago put the figure at around 20% in the average herd. While various nutrition and management options exist to reduce the incidence of anoestrus cows, when faced with large numbers of anoestrus cows immediately prior to MSD, the reliance is on therapeutic intervention.

Over the last 6 years, because of EU restrictions on the use of Oestradiol Benzoate (OBD) in food producing animals, the NZ dairy industry has had to move away from previously relied upon Progesterone and ODB based treatment protocols to Progesterone, GnRH and Prostaglandin based programmes.

This paper summarises two groups of studies in NZ over the 2010/11 and 2012/13 seasons with the aims to investigate the efficacy of 6 different anoestrus cow treatment protocols in NZ lactating dairy cows.

Study Group 2010/11 – (Shephard, 2013)

In this study comparisons were made between the efficacies of programmes containing either a 1.0g progesterone device (DIB-V) or a 1.38g progesterone device (CIDR). Additionally the study also set out to determine the efficacy of inclusion of equine chorionic gonadotropin, (eCG), into progesterone-based anoestrous cow treatment protocols for New Zealand dairy cows.

Methods

Anoestrous cows (n=1,906) from 12 herds were randomly assigned to four treatment groups as follows:

Group 1 - (GPG group, n= 475):

- 100 µg gonadorelin (GnRH) by IM injection at Day -10;
- 500 µg cloprostenol by IM injection at Day -3;
- 100 µg GnRH by IM injection at Day -1
- Fixed time artificial insemination (FTAI) on Day 0

Group 2 – (CIDR group, n= 477):

As for the GPG group above with a CIDR device (1. 38 g progesterone) inserted between Day -10 and Day -3

Group 3 - (DIB-V group, n=477):

As for the GPG group above with a DIB device (1.0 g progesterone) inserted between Day -10 and Day -3

Group 4 - (DIB + eCG group, n=477)

As for the DIB-V group above with 400 IU eCG by IM injection at Day -3

Statistical Analyses

Conception rates to FTAI and 4wk in calf rates were analysed using generalised estimating equations (GEE). Time to conception and time to return to oestrus were analysed using Kaplan Meier survival analysis and Cox's proportional hazards regression.

Results

Progesterone device retention rates were high for DIB-V (98.6%) and CIDR (99%) devices with no significant difference between retention rates of the two devices.

FTAI pregnancy rates are presented in Table 1. From modelling; Friesian cows, cows with BCS <4.0, cows inseminated on Day 0 and cows calved less than 60 days at mating start date (MSD) had lower conception rates than non-Friesian cows, cows BCS 4.0+, cows inseminated to detected heat and cows calved greater than 60 days at MSD. In cows calved less than 60 days at MSD all treatments performed similarly. In cows calved greater than 60 days prior to MSD the GPG group tended to perform similarly to the CIDR and DIB groups while the DIB + eCG group performed significantly better than the other treatment groups.

Table 1. Proportion pregnant by treatment group.

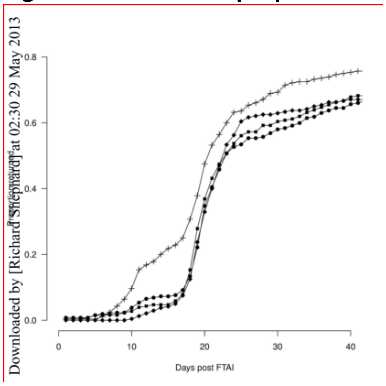
		FTAI			4 weeks		
	n	Proportion	Lower CI (95%)	Upper CI (95%)	Proportion	Lower CI (95%)	Upper CI (95%)
GPG	475	0.34	0.29	0.37	0.55	0.51	0.6
CIDR	477	0.38	0.34	0.43	0.57	0.52	0.61
DIB	477	0.38	0.33	0.42	0.56	0.52	0.6
DIB + eCG	477	0.41	0.37	0.46	0.63	0.59	0.67

Pregnancy rates at 4 weeks are presented in Table 1. The same breed, BCS, time of insemination, days calved and days calved by treatment effects noted at FTAI persisted to 4 weeks.

Cumulative proportions of cows conceiving by treatment groups are presented in figure 1. There was no significant difference in the survival distribution functions between treatment groups. ($\chi 2$ = 7.05, df=3 , p=0.070)

Cox's proportional hazards model demonstrated impacts of breed, days calved and age on time to conception. Friesian cows, cows calved less than 60days at MSD and cows outside of the age range 4-6yrs took longer to conceive than other cows.

Figure 1. Cumulative proportion of cows conceiving relative to MSD by treatment group.



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Conclusions & Relevance

The inclusion of eCG into progesterone-based anoestrous cow treatment protocols improves conception to FTAI and 28-day pregnancy rates in cow s >60 days calved at treatment compared with a GPG protocol.

There was no difference in clinical performance between DIB and CIDR devices.

The combination of a low payload (1.0 g) progesterone releasing intravaginal device with eCG treatment at device removal within a GPG treatment is a clinically effective treatment for anoestrous in New Zealand dairy cows.

Study Group 2012/13

Introductory comments

The use of equine chorionic gonadotropin (eCG) at progesterone insert removal (day 7) has been shown to improve pregnancy outcomes for non-cycling cows above.

Recent data from South America showed improved in-calf rates following anoestrous cow treatments in *Bos taurus* x *Bos indicus* suckling beef cattle when cows were given 400IU eCG 14 days following AI (Cutaia et al, 2012, NPR). Another South American study also demonstrated improved in-calf rates in lactating Holstein cattle following administration of 400IU eCG given 22 days after artificial insemination (AI). (Bartholomea et al, 2012). The increased in-calf rates appeared to be a combination of improved conception rates at fixed time AI as well as decreased embryonic loss rates.

This aims of these studies are to evaluate the efficacy of 4 different anoestrus treatment protocols on pregnancy rates of NVO cows under New Zealand dairy farming conditions.

Materials and Methods

The studies enrolled 2,661 spring calving anoestrus lactating dairy cows from 23 commercial dairy herds geographically spread throughout NZ.

All cows remained on their farm of origin throughout the study and were managed in accordance with generally accepted pastoral dairy farming practices.

Study 1. DIB Synch Plus cf DIB Synch Plus + 14deCG (n=1646 cows, n_f=23 farms)

On each farm the enrolled cows were randomly assigned to one of two treatment groups:

Group 1 DIB-Synch Plus:

Cows were treated on Day -10 with 100µg Gonadorelin by IM injection and with an intravaginal device containing 1g Progesterone (DIB-V).

On Day -3 the DIB-V was removed, and 500µg cloprostenol and 400IU eCG administered by IM injection. Cows were inseminated to observed heat from this time forward.

On Day -1 all cows not yet inseminated were treated with 100µg gonadorelin IM.

On Day 0 (MSD) all cows not yet inseminated were inseminated 16-20hrs after the 2nd gonadorelin injection.

Group 2 DIB-Synch Plus eCG 14d:

Cows were treated in the same manner as Group 1 cows with the additional treatment of 400IU eCG administered IM on Day 14.

Study 2. DIB Synch Plus cf DIB 0.5 Synch Plus (n=1002 cows, n_f=16 farms)

Group 1 DIB-Synch Plus (n=511) – treated as described above

Group 2 DIB 0.5 Synch Plus (n=491) – treated as for Group 1 with the substitution of a DIB 0.5 for the DIB-V

Study 3. DIB Synch Plus cf DIB Synch Plus ½ GnRH (n=848 cows, n_f=14 farms)

Group 1 DIB-Synch Plus (n=427) – treated as described above

Group 2 DIB Synch Plus ½ GnRH (n=421) – treated as for Group 1 with the substitution of a 50ug dose of gonadorelin for the 100ug dose of gonadorelin

Statistical Analysis

All data was collated into a spreadsheet (Microsoft Excel 2010, Microsoft Corporation Ltd) for subsequent manipulation and analyzed in XLStat 2013.3.04 ©Addinsoft 1995-2013.

Groups were assessed for homogeneity using Chi Square and t-test of means as appropriate on the basis of age, breed, BCS, Days Calved by MSD and Farm.

Contingency tables were constructed for single variables impact on treatment outcomes and analyzed using Chi square analysis to assist modeling. Cumulative pregnancy proportion curves were plotted for outcomes by treatment group, BCS category (<4 cf ≥4), age category (2y, 3y, 4-8y, ≥9y) and Days Calved by MSD category (<60d cf ≥60d). Kaplan-Meier analysis was used to evaluate differences in treatment outcomes. A Cox's Proportional Hazards model was used to assess impacts of individual predictor variables.

Results

Retention rate for the DIB-V devices was recorded as 99.3% in study 1. 1.3% of the DIB devices rotated in the vagina so that the tail was not apparent at removal.

Study 1.

Table 1 presents pregnancy proportions following MSD. There was no significant difference in pregnancy proportion at any time point.

Figure 1 depicts cumulative pregnancy proportions by treatment group. While there was a tendency for DIB Synch Plus treated cows to have higher cumulative pregnancy proportions for the 1st 6 weeks than DIB Synch Plus +14d eCG treated cows, this was not a significant result. (p = 0.184)

Mean survival to conception was 28.3 days (*95%CI = 26.0 – 31.0*) for DIB-V Synch Plus and 29.6 days *(95%CI = 27.2 – 32.0)* for DIB-V Synch Plus +14d eCG. These differences are not significant *(Wilcoxon test statistic 1.503, p = 0.220, α = 0.05).*

Significant effects of BCS, Age and Days calved by MSD were apparent and are summarized in Table 1. In particular 3yo cows performed well and the 9yr+ cows performed relatively poorly. 9yr+ cows had a higher relative risk of calving closer to MSD and being in poorer body condition at Day -10. Refer to Table 2. No effects of treatment by the above covariate interactions have been identified in the dataset at the time of writing.

Table 1. Number of cows pregnant, proportion pregnant and 95% confidence interval for proportion pregnant at FTAI, by 28 days and by 42 days post FTAI

		FTAI					28d					42d				
Treatment	Number	Preg.	Propn.	*Lower 95% CI*		*Upper 95% CI*	Preg.	Propn.	*Lower 95% CI*		*Upper 95% CI*	Preg.	Propn.	*Lower 95% CI*		*Upper 95% CI*
DIB Synch Plus	753	353	0.47	*0.43*	-	*0.50*	489	0.65	*0.62*	-	*0.68*	565	0.75	*0.72*	-	*0.78*
DIB Synch Plus +14d eCG	750	323	0.43	*0.40*	-	*0.47*	468	0.62	*0.59*	-	*0.66*	541	0.72	*0.69*	-	*0.75*
BCS <4	398	167	0.42	*0.37*	-	*0.47*	238	0.60	*0.55*	-	*0.65*	270	0.68^{a}	*0.63*	-	*0.72*
BCS ≥4	1185	538	0.45	*0.43*	-	*0.48*	762	0.64	*0.62*	-	*0.67*	883	0.75^{b}	*0.72*	-	*0.77*
Days Calved by MSD <60	529	201	0.38^{a}	*0.34*	-	*0.42*	288	0.54^{a}	*0.50*	-	*0.59*	345	0.65^{a}	*0.61*	-	*0.69*
Days Calved by MSD ≥60	996	484	0.49^{b}	*0.45*	-	*0.52*	682	0.68^{b}	*0.66*	-	*0.71*	775	0.78^{b}	*0.75*	-	*0.80*
Age Category																
2yo	360	161	$0.45^{a,b}$	*0.40*	-	*0.50*	226	$0.63^{a,b}$	*0.58*	-	*0.68*	275	$0.76^{a,b}$	*0.72*	-	*0.81*
3yo	320	164	0.51^{a}	*0.46*	-	*0.57*	225	0.70^{a}	*0.65*	-	*0.75*	250	0.78^{a}	*0.74*	-	*0.83*
4-8yo	810	355	0.44^{b}	*0.40*	-	*0.47*	505	0.62^{b}	*0.59*	-	*0.66*	577	0.71^{b}	*0.68*	-	*0.74*
9+yo	88	25	0.28^{c}	*0.19*	-	*0.38*	44	0.50^{c}	*0.40*	-	*0.60*	49	0.56^{c}	*0.45*	-	*0.66*

a, b – Within treatment groups, treatments with different superscripts differ (p < 0.05)

Figure 1. Cumulative Pregnancy Proportion by Treatment Group

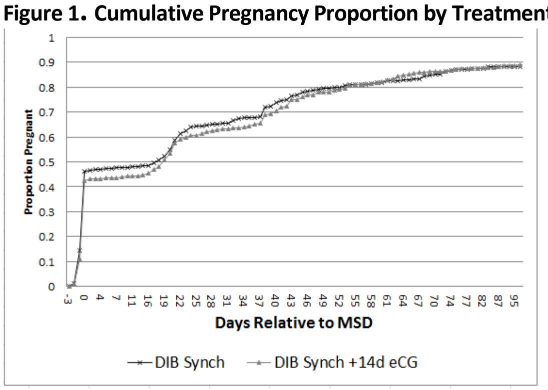


Table 2. Relative risk of being less than BCS 4 and calved <60days ay MSD by age category

	2yo	3yo	4-8yo	≥9yo
BCS <4	0.74	1.00	0.88	1.27
Days Calved by MSD <60	0.38	1.00	1.00	1.33

There was also significant variability in days to conception between different farms.

Study 2.

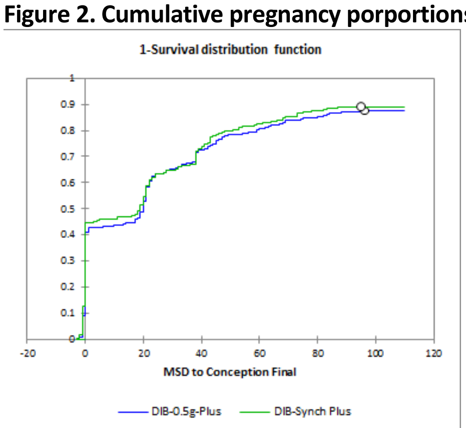
Table 3 presents pregnancy proportions following MSD. There was no significant difference in pregnancy proportion at any time point.

Table 3. Pregnancy Proportion and Confidence Intervals for DIB-0.5g-Plus v DIB-Synch Plus

		FTAI			4week			6week			12week		
	n	Propn.	Lower CI 95%	Upper CI 95%	Propn.	Lower CI 95%	Upper CI 95%	Propn.	Lower CI 95%	Upper CI 95%	Propn.	Lower CI 95%	Upper CI 95%
DIB-0.5g-Plus	491	0.43	*0.38*	*0.47*	0.65	*0.61*	*0.69*	0.74	*0.70*	*0.78*	0.87	*0.84*	*0.90*
DIB-Synch Plus	511	0.45	*0.41*	*0.50*	0.65	*0.60*	*0.69*	0.75	*0.72*	*0.79*	0.89	*0.86*	*0.91*

Figure 2 depicts cumulative pregnancy proportions (1-SDF) by treatment group. While there was a tendency for DIB Synch Plus treated cows to have higher cumulative pregnancy proportions for the 1st 3 weeks than DIB 0.5 Synch Plus treated cows, this was not a significant result. (p > 0.25)

Figure 2. Cumulative pregnancy porportions (1-SDF) for DIB 0.5 Synch Plus and DIB Synch Plus treated cows



Mean survival to conception was 26.4 days (*95%CI = 23.6 – 29.2*) for DIB Synch Plus and 28.2 days *(95%CI = 25.2 – 31.2)* for DIB 0.5 Synch Plus.

There was a positive effect of having BCS 4.0+, days calved at MSD and being a 3yo on conception rates. No effects of treatment by the above covariate interactions have been identified in the dataset at the time of writing.

Again farm variability in conception rates was high.

Study 3.

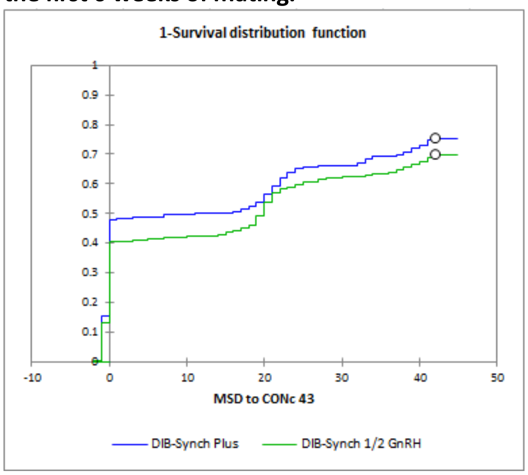
Table 4 presents pregnancy proportions following MSD. There was a significant difference at FTAI favouring the full 100ug dose of GnRH in the DIB Synch Plus group. (Chi square p = 0.021, df = 3).

Table 4. Pregnancy Proportion for DIB-Synch 1/2 GnRH and DIB-Synch Plus

		FTAI			4week			6week			12week		
	n	Propn.	Lower CI 95%	Upper CI 95%	Propn.	Lower CI 95%	Upper CI 95%	Propn.	Lower CI 95%	Upper CI 95%	Propn.	Lower CI 95%	Upper CI 95%
DIB-Synch 1/2 GnRH	421	0.41 a	*0.36*	*0.46*	0.62	*0.57*	*0.66*	0.70	*0.65*	*0.74*	0.86	*0.83*	*0.89*
DIB-Synch Plus	427	0.49 b	*0.44*	*0.53*	0.66	*0.62*	*0.71*	0.75	*0.71*	*0.79*	0.87	*0.84*	*0.91*

Figure 3 depicts cumulative pregnancy proportions (1-SDF) by treatment group over the first 6 weeks of mating. There was a very strong tendency for DIB Synch Plus treated cows to have higher cumulative pregnancy proportions for the 1st 6 weeks than DIB Synch Plus ½ GnRH treated cows. (Wilcoxon test statisitic 3.808, p=0.051, α=0.05)

Figure 3. Cumulative Pregnancy Proportion (1-SDF) for DIB Synch Plus and DIB Synch Plus ½ GnRH treated cows over the first 6 weeks of mating.



Mean survival to conception was 25.8 days (*95%CI = 22.7 – 29.0*) for DIB-V Synch Plus and 29.4 days *(95%CI = 26.2 – 32.7)* for DIB-V Synch Plus ½ GnRH over the whole mating period. These differences are not significant *(Wilcoxon test statistic 3.184, p = 0.074, α = 0.05).*

Being of BCS 4.0+ was associated with a positive impact on pregnancy proportion. No effects of treatment by other covariate interactions have been identified in the dataset at the time of writing.

Again there was variability in conception rates between farms.

Discussion and Clinical Relevance

The results of Study 1 do not support the addition of an extra treatment of 400IU of eCG administered 14 days after A.I. to improve in-calf rates over and above that achieved by using a P4+GPG+eCG (DIB-V Synch Plus) programme in anoestrus dairy cows in NZ.

This contrasts with the results of Bartholomea et al (Bartholomea et al, 2012) who found that 400IU eCG administered IM 22 days post-AI increased fertility, particularly in lower BCS cows. These results also contrast with the results of Cutaia et al (Cutaia et al, 2012, NPR) who demonstrated a positive effect at FTAI in-calf rates (P = 0.02) of eCG administered 14days after A.I. to anoestrus (n= 260, 11% CL positive by rectal ovarian palpation) beef cattle. (+14d eCG: 60/127, 47.2% and no eCG: 41/133, 30.8 %).

Older cows (9yr+) performed poorly in this study. However the impacts of later calving dates and poorer BCS offset the relatively poor response to treatment. Caution should therefore be exercised when interpreting these results. A blanket recommendation not to submit older cows for treatment for example is not supported by the results of this study.

Days calved before MSD had the largest impact on mean survival to pregnancy underlining the importance of maintaining tight calving patterns in the NZ dairying environment.

The results of Study 2 support the use of a very low payload of progesterone (DIB 0.5, 0.5g progesterone) for treatment of anoestrus cows in the NZ dairy environment. This is in alignment with field extension of the findings of Videla et al (2008) who demonstrated equivalence of plasma progesterone profiles following insertion of either a 1.0g (DIB-V) or a 0.5g (DIB 0.5) progesterone device.

The results of Study 3 do not support the reduction to 50µg of the standard 100µg dose of gonadorelin used in current GPG+P4 anoestrus treatment programmes in NZ dairy cows.

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