HERITABILITY OF PLASMA CONCENTRATIONS OF IGF1 AND ITS CORRELATION WITH REPRODUCTIVE PERFORMANCE IN HOLSTEIN COWS IN VICTORIAN HERDS

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SUMMARY

Compromised cow fertility is a significant cause of productivity loss in the dairy industry. It is hard to measure accurately, and has low heritability, but can be improved through selection of correlated traits with greater heritability. Plasma concentration of insulin-like growth factor-1 (IGF1) has recently been identified as a possible indicator trait for fertility. To investigate this further, the heritability of plasma IGF1 and its correlation with reproductive performance were measured in a group of 3700 Holstein cows from 22 commercial dairy herds in Victoria. Heritability was moderate for IGF1 (0.23 ± 0.05) but low for reproduction traits (0.06 – 0.10) even though between-cow variation was high. Genetic correlations between IGF1 and reproductive outcomes could not be estimated. Phenotypic correlations between IGF1 and reproductive outcomes were low and positive, but significant. Pearson's correlation coefficients between sire Australian Breeding Values for fertility had moderate positive correlations with sire best linear unbiased prediction solutions for IGF1, suggesting a moderate genetic correlation exists. Analysis of Variance between IGF1 and reproductive outcomes also showed a positive relationship between IGF1 and oestrus and conception. These results suggest that in the pasture-based dairying systems of Victoria, plasma concentrations of IGF1 could be gradually altered by genetic selection. Any associated affects on fertility would be positive, but minor.

INTRODUCTION

Continual breeding for high milk production in dairy cows has lead to physiological changes associated with declining fertility. Compromised fertility is a significant area of productivity loss. Improving it through genetic selection is difficult as fertility is hard to measure accurately and has low heritability. Plasma concentrations of insulin-like growth factor-1 (IGF1) could be used as a tool to improve cow fertility (Moyes 2004). Plasma IGF1 is related to the reproductive performance of the dairy cow due to its association with the partitioning of nutrients among biological functions (Bauman and Currie 1980) and its direct stimulatory affects on the ovaries (Spicer *et al.* 1993). IGF1 stimulates ovarian granulosa cell proliferation and mitogenesis, enhancing steroidogenesis by granulosa cells, and stimulating progesterone production (Spicer *et al*. 1993). Plasma concentrations of IGF1 are sensitive to nutrition, and the negative energy balance that dairy cows experience in early lactation is associated with low plasma IGF1 concentrations (Sharma *et al*. 1994). Therefore, IGF1 is considered to be a mediator of the effects of nutrition on reproduction, and has been associated with the resumption of cyclic activity in early lactation both overseas (Lucy *et al*. 1992; Beam and Butler 1998) as well as in Australia (Obese 2003; Moyes 2004). Previous studies involving IGF1 in dairy cows have only investigated phenotypic relationships. Moderate negative genetic and phenotypic correlations between IGF1 and milk production have been demonstrated for the group of cows in this study (Stirling *et al*. 2008). The aim of this study was to derive heritability estimates for plasma IGF1 in Holsteins in Victorian herds as well as genetic and phenotypic associations between IGF1 and reproductive performance. The findings could provide information to allow the industry to balance the need to maintain its commercial competitiveness by increasing milk yield without sacrificing fertility.

MATERIALS AND METHODS

Herds. Twenty-two commercial dairy herds throughout Victoria were involved in the study. Herd selection criteria included: predominantly Holstein genetics, consistent use of semen from the progeny testing program of Genetics Australia; good records and safe facilities. Herds were classified into one of two "systems" referring to calving management i.e. "seasonal" (single calving period each year) and "split" (multiple calving periods each year). Herds were also classified by calving "season" referring to the time of year and year and in which that herd calved, for example "Spring 2005" and "Autumn 2006".

Reproduction. Each herd bred cows during defined "breeding periods". Seasonal herds had one breeding period per year whereas split calving herds had two or three breeding periods per year. Mating start date (MSD) marked the beginning of each breeding period and usually occurred approximately 12 weeks after the start of the corresponding calving period. During the breeding period cows were artificially inseminated (AI'd) when they were detected in oestrus. Breeding periods varied in length between herds (typically ~9-12 weeks). Some herds introduced a bull into the herd at the end of the AI breeding period. Pregnancy testing typically occurred ~6 weeks after the end of AI. Reproductive performance was estimated using calving dates, AI dates and pregnancy test results. Parameters calculated included the interval (in days) between MSD to first AI and conception (MSD1stserv and MSDConc, respectively) for cows with positive reproductive outcomes. Binary outcomes for 3 and 6 week AI submission rates and 6 and 21 week in-calf rates were calculated as an indicator of oestrus and conception, respectively, at a given number of weeks after MSD (for all cows; both positive and negative reproductive outcomes).

Sampling and assays. Blood samples were collected from the tail vein of each enrolled cow during the dry period (Dry) and around MSD. Samples were placed on ice immediately, centrifuged at 1800 x g for 10 min, and plasma frozen at -20ºC until assays were undertaken. Concentrations of total plasma IGF1 was measured using the DSL-10-2800ACTIVETM Non-extraction IGF1 ELISA (Diagnostic Systems Laboratories, Webster, Texas, USA) in the laboratories of Primegro Ltd, Adelaide, using the method of Obese *et al*. (2008). Inter-assay variation (CVs) ranged from 4.3% to 6.9%, and mean intra-assay variation from 3.0% to 4.5%.

Data analyses. Heritabilities and genetic correlations of IGF1 and reproductive performance were calculated using ASReml (Gilmour *et al*. 2006). An animal model was used, utilising pedigree information from each cow's dam, sire and maternal grand-sire. Approximately 3700 cows of $\geq$ second parity were included in the analyses. Univariate analyses were performed to estimate heritabilities and confirm the suitabilities of models used for each trait. Bivariate analyses were performed to obtain estimates of genetic correlations. Contemporary groups of cows were constructed from the concatenation of calving system, herd and recording date as these were not cross-classified effects. Linear covariates for the intervals between drying off and sampling and sampling to calving were fitted for dry IGF1. A linear covariate for days in milk at sampling was fitted for MSDIGF1. Cow age was fitted as a yearly class effect, with cows 10 years or older grouped together into the same class. Models for IGF1 traits were redefined to accommodate herd, sampling date and IGF1 assay batch/plate effects. Best linear unbiased prediction (BLUP) solutions for IGF1 in sires were also calculated, and correlated with sire Australian Breeding Values (ABVs) for fertility using Pearson's correlations. Sire ABVs were obtained from a recent genetic evaluation by the Australian Dairy Herd Improvement Scheme, which used data from all daughters and herds, rather than just herds recorded in this study, giving a relatively high

reliability for fertility (84%). The relationship between IGF1 and binary reproductive outcomes for oestrus and conception were analysed with ANOVA using residuals for IGF1 that had been adjusted for herd, season, age, sampling date and IGF1 assay batch/plate effects.

RESULTS AND DISCUSSION

Means, variation and heritability estimates for each trait are outlined in Table 1. Means and variation of plasma IGF1 were similar to that reported in other studies involving pasture-fed dairy cows (Obese 2003; Moyes 2004), lower than that recorded for beef cattle (Johnston *et al.* 2001), but higher than that reported for dairy cows fed total mixed rations (Beam and Butler 1998). Plasma IGF1 had a moderate heritability (0.23), which is within the range of 0.18 to 0.48 that has been reported for dairy and beef cattle in other studies (Davis and Simmen 2000; Grochowska *et al*. 2001; Johnston *et al*. 2001). Means for fertility traits suggest a substantial decline in fertility in Victorian dairy herds since a large field study by Morton (2000). The heritability of fertility traits was low ($\leq$ 0.10; Table 1). This was similar to most international studies in dairy cows (Grosshans *et al.* 1997; Pryce *et al.* 1998; Berry *et al.* 2003). Fertility is difficult to measure as the phenotypic outcome depends on many non-genetic factors, ie. environmental and management factors. This is why it may be more effective to improve the genetic potential of fertility by selecting for traits with higher heritabilities that are known to be associated with fertility.

Table 1. Means, coefficient of variation (CV), heritability (h^2) and phenotypic variation (σp) of plasma IGF1 measured at the dry period (Dry) and mating start date (MSD), the interval between MSD and first service (MSD1stserv) and MSD and conception (MSDConc), 3 and 6 week submission rates (3 wk Sub, 6 wk Sub), and 6 and 21 week conception rates (6 wk Con, 21 wk Con).

	Mean ± SD	CV	h^2 ± SE	σp
Dry IGF1 (ng/ml)	154.0 ± 60.2	39	0.23 ± 0.05	43.8
MSD IGF1 (ng/ml)	89.4 ± 39.0	44	0.23 ± 0.05	33.7
MSD1stserv (days)	19.0 ± 28.4	149	0.06 ± 0.04	24.3
MSDConc (days)	46.9 ± 57.3	122	0.10 ± 0.05	49.8
3 wk Sub (%)	0.70 ± 0.46	-	0.03 ± 0.02	0.40
6 wk Sub (%)	0.88 ± 0.33	-	0.09 ± 0.04	0.28
6 wk Con (%)	0.55 ± 0.50	-	0	0.46
21 wk Con (%)	0.78 ± 0.41	-	0.02 ± 0.03	0.37

SD = standard deviation, SE = standard error

Most fertility traits failed to converge in bivariate analyses because of very low heritabilities (when estimable) under univariate analyses. For MSD1stserv the genetic variance was forced to the zero boundary so that a genetic correlation was not estimable. Phenotypic correlations were only obtained between MSDIGF1 and MSD1stserv (-0.11 ± 0.02; correlation ± standard error) and MSDIGF1 and MSDConc (-0.06 ± 0.02). This suggested that higher IGF1 was associated with slightly reduced intervals to conception and a higher probability of observing oestrus soon after MSD (phenotypically). ANOVA between residuals for IGF1 and binary reproductive outcomes showed that cows that showed oestrus and were inseminated in the first 3 and 6 weeks after MSD had higher IGF1 (Dry and MSD) than cows that were not ($p<0.05$). Cows that conceived in the first 6 and 21 weeks after MSD had numerically greater IGF1 than cows that did not, but this was only statistically significant for the 6 week conception rate with MSDIGF1. Pearson's correlation coefficient between sire ABVs for fertility and sire BLUP solutions for IGF1 was 0.26 for Dry IGF1 and 0.16 for MSD IGF1. This gave further information on the positive genetic relationship

between IGF1 and fertility, given the higher reliability of fertility data using greater numbers of animals in the ADHIS database to calculate ABV for fertility.

CONCLUSIONS

In the herds studied, plasma IGF1 concentrations displayed moderate variation and moderate heritability. Fertility traits had high variation (phenotypic) but low heritability. Genetic correlations between IGF1 and reproductive performance could not be demonstrated with this dataset. A moderate genetic relationship was demonstrated between sire BLUP solutions for IGF1 and sire ABVs for fertility. The phenotypic relationship between IGF1 and reproductive performance was positive, but weak. These results suggest that in Victorian dairy systems, IGF1 could be gradually altered by genetic selection, but the affect on fertility would probably be small. Given the negative genetic correlation between milk yield and IGF1 previously shown, further investigations could examine the use of IGF1 in a multi-trait selection index, or the relationship between sire IGF1 and daughter fertility to improve the reliability of sire ABVs for fertility.

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