

Genetic and Genomic Analysis of Superovulatory Response in Canadian Holsteins

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Abstract

Superovulation of dairy cattle is frequently used in Canada. The cost of this protocol is high, and so is the variability of the outcome. Knowing the superovulatory potential of a donor cow could influence the breeder's decision to superovulate it or not. The main objective of this study was to perform a genetic and genomic analysis for superovulatory response of Holstein cows in Canada, using data recorded by Holstein Canada. Data contained the total number of embryos and the number of viable embryos from every successful flushing performed across Canada. After editing, 137,446 records of superovulation done between 1992 and 2014 were considered for the analysis. A univariate repeatability animal model analysis was performed for both total number of embryos and number of viable embryos. As both data and residuals for total number of embryos and number of viable embryos did not follow a normal distribution, records were transformed using either logarithm transformation or Anscombe transformation. Using log transformation heritability estimates (SE) of 0.15 (0.01) and 0.14 (0.01) were found for total number of embryos and number of viable embryos, respectively. Using Anscombe transformation the heritability estimates (SE) were 0.17 (0.01) and 0.14 (0.01) for total number of embryos and number of viable embryos, respectively. Estimated breeding values of sires with reliabilities higher than 40% were used for calculating correlations between estimated breeding values and other routinely evaluated traits. The results showed that selection for a higher response to superovulation would lead to a slight decrease in production, but an improvement for functional traits, including all reproduction traits, however in all cases the estimated correlations are either low or modest. Considering the results obtained in this study, genetic selection for increased superovulatory response in donors is possible. Preliminary results from a genome-wide association study showed that one big region on chromosome 11 seems to be associated with superovulatory response, but more research is needed to confirm this finding.

Key words: superovulation, embryo production, genetic parameter, breeding value

Introduction

The production of embryos from superovulated females is important for the dairy industry in Canada. As reported by the International Embryo Transfer Society, in 2013, there were a total of 340,000 dairy embryos produced in vivo worldwide, being about 20% produced in Canada, making Canada the second biggest producer of in vivo dairy embryos (International embryo transfer society, 2013). Currently about 15% of the Canadian embryo production is exported each year, to many countries around the world, for a total value of around 8 million dollars (CAD) per year (Canadian Dairy Information Center, 2015).

Production of embryos from superovulated females is associated with some opportunities, but also some challenges. The variability of superovulatory response is an issue that has been addressed by many authors (Hahn, 1992; Kanitz *et al.*, 2002; Lonergan and Boland, 2011). While some donors may produce up to 50 embryos, about 10 to 20% of donors will have unsuccessful flushes (Boviteq, Quebec, Canada, personal communication). Considering this variability and the high cost of superovulation and embryo transfer, some breeders choose not to use this technique even though it could greatly improve the genetic gain of their herds. To date, there have been no genetic or genomic analyses performed for superovulatory response in Canada.

The objectives of this study were, therefore, to estimate genetic parameters and breeding values for superovulatory response traits, examine their relationship with other routinely evaluated traits in Canada, and perform a preliminary genome-wide association study on these traits.

Materials and Methods

Data

The data set used in this study was provided by Holstein Canada and originally contained 168,855 records from 1980 to 2014. After editing, it contained 137,446 records from 1992 to 2014. One particularity of this data set is that it only contained records from successful flushes. Therefore, only records with at least one embryo produced were available. Only complete and unique records were used, records were kept only if the donor was between 8 and 180 months of age at recovery, and only records from clinics with at least 50 records were considered.

Two superovulatory response traits were available in the data set, namely the total number of embryos (**NE**) and the number of viable embryos (**VE**). The total number of embryos included all the embryos recovered from a flush, even dead or degenerated embryos, while the number of viable embryos only included the embryos that were reported to Holstein Canada as transplanted or frozen.

Data transformation

As both data and residuals for NE and VE did not follow a normal distribution, records were transformed using either logarithm (log) transformation or Anscombe (ans) transformation, as follows:

$$NE_{\log} = \ln(NE)$$

$$NE_{ans} = 2 \times \sqrt{(NE + (3/8))}$$

$$VE_{\log} = \ln(VE + 1)$$

$$VE_{ans} = 2 \times \sqrt{(VE + (3/8))}$$

Models

Univariate repeatability animal model were used to analyze the data, using the average information-restricted maximum likelihood (AI-REML) procedure in the derivative-free approach to multivariate analysis in DMU package (Madsen and Jensen, 2008).

Univariate linear model

Univariate analyses were run for both superovulatory response traits, using the following model:

$$y = X\beta + Z_d d + Z_{ss} ss + Z_{pe} pe + e,$$

where y is a vector of observations for NE or VE; β is a vector of systematic effects, including fixed effects of age (as linear and quadratic covariate) nested within service type, year-month of recovery, clinic-year of recovery, and service type; d is a vector of random animal additive genetic effects of the donor cow; ss is a vector of random animal additive genetic effects of the service sire; pe is a vector of random permanent environmental effects of the donor; e is a vector of random residuals; and X , Z_d , Z_{ss} and Z_{pe} are the corresponding incidence matrices.

Genome-wide association study

To perform the genome-wide association study, the single-SNP regression method was used in snp1101 software (Mehdi Sargolzaei, personal communication). Only animals that were genotyped with at least a 50K SNP chip panel were included in the analysis, and all the genotypes were imputed to HD using FImpute (Sargolzaei *et al.*, 2014). De-regressed EBVs were used with a threshold of reliability of 10%, leaving 3,423 cow and 763 sires to be considered in the analysis.

Results and Discussion

Descriptive statistics

Table 1 includes the descriptive statistics of the data set. Mean values for NE and VE were 9.2 and 7.6, respectively. Those values were higher than previous estimates reported by other studies, likely because the data set in the current study did not include the unsuccessful flushes.

Table 1. Summary statistics of the data (NE = total number of embryos, VE = number of viable embryos).

| | Total (N) | Mean | SD | Min | Max |
|---------------|-----------|------|------|-----|-----|
| Records | 137,446 | - | - | - | - |
| Donors | 54,463 | - | - | - | - |
| Sires | 3,513 | - | - | - | - |
| Service sires | 2,250 | - | - | - | - |
| Clinics | 100 | - | - | - | - |
| NE | 1,265,333 | 9.21 | 7.24 | 1 | 87 |
| VE | 1,044,416 | 7.60 | 5.92 | 0 | 58 |

Genetic parameters

The estimated genetic parameters for both traits by the univariate analyses are presented in Table 2. For both traits and using logarithmic or Anscombe transformation, the heritability for the donor effect was between 0.14 and 0.17. Heritability for the effect of service sire was very low for both superovulatory response traits using either transformation. These results are in accordance with previous studies (Bényei *et al.*, 2004; König *et al.*, 2007; Merton *et al.*, 2009; Tonhati *et al.*, 1999).

Table 2. Heritabilities for the donor effect (h_d^2) and the service sire effect (h_{ss}^2) from univariate analyses for the total number of embryos (NE) and the number of viable embryos (VE) using either logarithmic (Log) or Anscombe (Ans) transformation of the data (SE in parentheses).

| | Trait | h_d^2 | h_{ss}^2 |
|-----|-------|---------------|---------------|
| Log | NE | 0.148 (0.007) | 0.007 (0.001) |
| | VE | 0.135 (0.007) | 0.014 (0.002) |
| Ans | NE | 0.174 (0.008) | 0.006 (0.001) |
| | VE | 0.144 (0.007) | 0.014 (0.002) |

Correlation between estimated breeding values

EBV correlations between superovulatory response traits and other routinely evaluated traits in Canada were calculated using the EBV of sires that had reliability equal or higher than 40% (Table 3). Given that EBV from the log transformed and Anscombe transformed data were highly correlated (0.98), only results from the log transformed data are presented hereafter.

Both, NE and VE, had similar estimated correlations with routinely evaluated traits. There was a weak negative correlation between superovulatory response traits and LPI (Lifetime Performance Index; Canada’s national selection index), implying that current global selection in Canada will tend to slightly decrease the number of embryos produced by Holstein cattle over time. Similarly, EBV correlations with production traits were also weak and negative, implying that high producing dairy Holstein should tend to produce fewer embryos when superovulated. Finally, superovulatory response was positively correlated with reproduction traits. This was expected considering that superovulation is also related to reproduction. Overall, all EBV correlations were low, indicating that superovulatory response is a unique trait in the sense that it provides new information, which is not currently recorded via other traits in the Canadian dairy industry.

Table 3. Pearson correlations between EBV of sires from univariate analyses with a minimum reliability of $\geq 40\%$ for total number of embryos (NE; n=1,391) and number of viable embryos (VE; n=1,251) and EBVs of routinely evaluated traits.

| Trait | NE | VE |
|---------------------------------------|----------|----------|
| LPI | -0.23*** | -0.14*** |
| Milk yield | -0.26*** | -0.21*** |
| Protein yield | -0.29*** | -0.24*** |
| Fat yield | -0.21*** | -0.15*** |
| Daughter fertility | 0.20*** | 0.20*** |
| 56-d non-return rate | 0.16*** | 0.15*** |
| Number of services | 0.20*** | 0.21*** |
| 1 st service to conception | 0.19*** | 0.20*** |
| Calving to first service | 0.12*** | 0.12** |
| Days open | 0.21*** | 0.21*** |

Significant effects: ** = P<0.01, *** = P<0.001.

Genome-wide association study

Figure 1 shows the results from the GWAS for the number of viable embryos. As the two superovulatory response traits were highly correlated, similar results were found for the total number of embryos. As shown in Figure 1, one big peak in a region on chromosome 11 seems to be associated with superovulatory response.

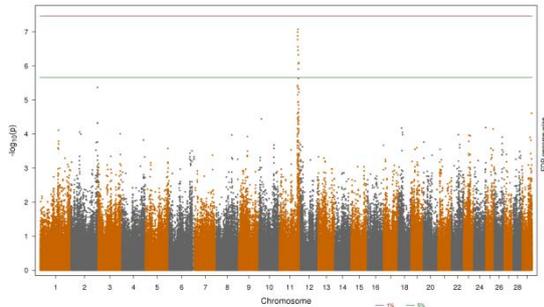


Figure 1. Manhattan plot from genome-wide association study for the number of viable embryos produced by superovulated Holstein donors.

Conclusions

This study confirmed that genetic selection for increased superovulatory response in Canadian Holstein is possible and that this trait is mostly uncorrelated with other traits routinely evaluated in Canada. One region on chromosome 11 was found associated with superovulatory response. More research will be needed to confirm this association and to find candidate genes associated with superovulatory response.

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