Longitudinal Effects of Muscular Hypertrophy Allele on Milk Production Traits During the Lactation Using a Novel Equivalent Model when Molecular Information is Limited

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Introduction

In Belgium, the dual purpose Belgian Blue breed (DP-BBB) is a vulnerable breed. The breeders currently still having DP-BBB animals mention several reasons. Besides, the traditional look and the link of DP-BBB to the landscape of the Walloon Region of Belgium, the DP-BBB animals are considered having good features (robustness, fertility and longevity), being ease to manage in general and having a good calving ease. Due to its dual purpose type, income generated by both milk and meat is more stable and more flexible in responding to market fluctuations.

An 11 bp-deletion within the exon 3 of the *Myostatin* gene (Grobet *et al*., 1997) causes the double muscling phenotype, the allele including this deletion is called mh (muscular hypertrophy) allele. Even if the mh allele frequency is close to 100 % in Belgian Blue beef type (the well known Double-Muscled Belgian Blue cattle), this frequency is only about 61 % in DP-BBB.

Given the importance of the effects of the mh allele on the conformation and the musculature and its potential indirect role in dairy production, it seemed interesting to consider its presence in genetic evaluation of the DP-BBB animals. Nevertheless, all the DP-BBB animals could not be genotyped. Therefore, a new alternative strategy was developed to allow the incorporation of molecular information available for a portion of the population.

Material and methods

Molecular data. The Walloon Breeding Association (AWE, Ciney, Belgium) provided genotype for 108 DP-BBB bulls and 1,891 DP-BBB cows. All animal were genotyped for the 11 bp-deletion in the *Myostatin* gene with a method adapted from Fahrenkrug *et al.* (1999).

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Quantitative data. Data used were provided by AWE for routine evaluation for milk production. These data included 11,117,505 test-day (TD) records for 689,057 dairy cows in production. The pedigree file contained 1,606,024 animals (cows with production records and ancestors). The genotyped animals had 11,150 daughters with TD records.

Statistical model. The model used was based on the multi-trait multi-lactation (3 traits x 3 lactations) model used for the routine evaluation for milk production in the Walloon Region (Auvray and Gengler, 2002). This model was slightly modified with an additional fixed effect, based on the genotype status for the mh allele.

Equivalent mixed inheritance model. Underlying hypothesis were based on the idea that knowledge of genotypes will not affect overall additive genetic variance but only change expected values of genetic effects for animals with known genotypes. The mixed inheritance model combining single gene effects or SNP, hereafter called ‘gene’ effect (g) and random polygenic effects (u) can be written as $\mathbf{y} = \mathbf{X}\boldsymbol{\beta} + \mathbf{ZQg} + \mathbf{Zu} + \mathbf{e}$, where $\mathbf{y}$ is a vector of data, $\boldsymbol{\beta}$ a vector of fixed effects, $\mathbf{X}$ and $\mathbf{Z}$ are incidence matrices linking effects and $\mathbf{y}$, and $\mathbf{Q}$ is a matrix linking gene effects and animals. A very simple equivalent model is $\mathbf{y} = \mathbf{X}\boldsymbol{\beta} + \mathbf{Zu}^* + \mathbf{e}$ where $\mathbf{u}^* = \mathbf{Qg} + \mathbf{u}$ and the basic assumptions are modified accordingly. Following Quaas (1988) and using the same strategy he used to integrate genetic groups, the following alternative mixed model equations allow the joint estimation of $\boldsymbol{\beta}$, $\mathbf{u}^*$ and $\mathbf{g}$:

$$\begin{bmatrix} \mathbf{X'R^{-1}X} & \mathbf{X'R^{-1}Z} & \mathbf{0} \\ \mathbf{Z'R^{-1}X} & \mathbf{X'R^{-1}Z+G^{-1}} & \mathbf{-G^{-1}Q} \\ \mathbf{0} & \mathbf{-Q'G^{-1}} & \mathbf{Q'G^{-1}Q} \end{bmatrix} \begin{bmatrix} \hat{\boldsymbol{\beta}} \\ \hat{\mathbf{u}}^* \\ \hat{\mathbf{g}} \end{bmatrix} = \begin{bmatrix} \mathbf{X'R^{-1}y} \\ \mathbf{Z'R^{-1}y} \\ \mathbf{0} \end{bmatrix}$$

Computations of the modified mixed model equations was done solving iteratively two subsystems of equations, one for the polygenic effects , except the gene effect, and one for the gene effect. Through modification of the system of equations the setup of the second subsystem did not require the knowledge of the genotype of all animals. Iterative solving of the two subsystems was done until the relative differences in the gene solutions were below 10^{-5}.

Results and discussion

Proportions of the three genotypes in the genotyped DP-BBB animals were as follows: 19.5 % +/+, 39.3 % mh/+ and 41.2 % mh/mh. The incorporation of this limited molecular data into this modified genetic evaluation allowed the estimation of the allelic substitution effect. As expected, the mh allele had negative effects on milk production traits. For the first three lactations, the average estimated allelic substitution effects (substitution of the wild-type allele by the mh allele) are presented in Table 1.

Table 1: Allelic substitution effect of the mh allele (g_s)$^{\alpha}$

Trait	g_s
Milk yield (kg / 305 d of lactation)	- 158.7
Fat yield (kg / 305 d of lactation)	- 8.93
Protein yield (kg / 305 d of lactation)	- 5.64
Fat content (%)	- 0.074
Protein content (%)	- 0.009

$^{\alpha}$ Allelic substitution effects were means of effects obtained for the first three lactations.

These effects are the same order of magnitude as the effects presented by Buske *et al.* (2010). Using a conventional mixed inheritance test-day model using externally estimated breeding values and their distribution as prior information, Buske *et al.* (2010) estimated additive effects of the mh allele for milk yield (-120.26 kg per lactation), for protein content (0.001 %) and for fat content (-0.02 %). The allelic substitution effect on the protein content close to zero could be explained by the fact that the phenotypic correlation between milk and protein yield was very high (> 0.96).

These alternative mixed model equations allowing the incorporation of limited molecular information offered the possibility, when applied on the random regression model used for the routine evaluation for milk production in Walloon Region and slightly modified as explained above, to model the gene effect through the first three lactations. As an example, Figure 1 presents the estimated allelic substitution effect of mh allele on daily milk yield through the first three lactations.

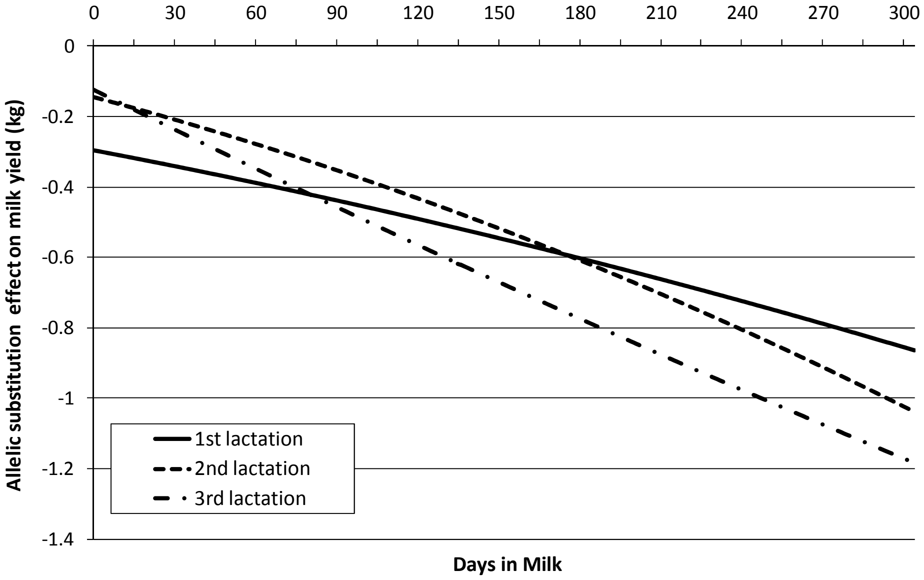

Figure 1: Estimated substitution effect of mh allele on daily milk yield through the first three lactations

The substitution effect of mh allele on milk yield was not constant throughout lactation. This effect was also variable for four other milk traits (data not shown). As observed in Figure 1, the substitution effects for protein yield and fat yield were also of increasingly important throughout each of the first three lactations. This was consistent with the fact that DP-BBB cows with a more meaty conformation (e.g., mh/mh genotype) seem to have less lactation persistency.

Conclusion

The mh allele which is favorable in meaty beef production exerts a negative effect on milk production traits of the dual purpose Belgian Blue cattle. This study also demonstrated the feasibility of integrating molecular information of a major gene and available for part of the population in a genetic evaluation model used routinely. This novel equivalent model allowed us to show that the effect of mh allele is variable during the first three lactations. Therefore, this will allow a better estimation of genetic potential in the case of breed with this kind of specificity (selection including a major gene).

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