THE EFFECT OF BOVINE MHC CLASS II POLYMORPHISM ON BULL BREEDING VALUES FOR CLINICAL MASTITIS AND SOMATIC CELL COUNTS IN MILK

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SUMMARY

The effects of class II genes within the BoLA DQ region on mastitis was analysed on 196 AI bulls of the Swedish Red and White breed. The bulls were DQ typed by use of restriction fragment length polymorphisms. The level of resistance was measured as breeding values of the bulls, constructed from progeny records on veterinary treatments and somatic cell counts respectively. Our previous analysis, based on breeding values for clinical mastitis only, showed that one of the haplotypes, DQ^{1A}, was significantly associated with lower breeding values for clinical mastitis. In the present analysis with updated breeding values, the significant effect of DQ^{1A} on clinical mastitis remained. However, no significant effect of DQ^{1A} on the breeding value for SCC was found. No other DQ haplotype showed any significant effect on any of the mastitis traits analysed.

INTRODUCTION

Mastitis is a disease with considerable effects on the economic outcome in milk production. Much effort has been made in trying to identify genetically determined mechanisms that could be used in selection for improved resistance. Genes of the major histocompatibility complex (MHC) have attended great interest during the last 10 years, due to their potential involvement in resistance to various diseases (for review see Klein, 1986). MHC has proven to be the most polymorphic gene region known at present and it has been identified in most species. The main function of the MHC is in the regulation of the immune response, including both B and T cells (for review see Klein, 1986). Within the bovine MHC (BoLA), two regions have been defined, class I (Amorena and Stone, 1978; Spooner et al. 1978) and class II (Usinger et al. 1977). The class II region has been further characterized at the molecular level by Andersson et al. (1986a, b; 1988), Andersson and Rask, (1988), Sigurdardóttir et al. (1988) and Groenen et al. (1989). There are indications on an effect of the BoLA region on resistance to mastitis (Solbu et al. 1982; Lundén et al. 1990).

In Sweden, breeding values for clinical mastitis, constructed from data on veterinary treatments, and for somatic cell counts (SSC) are provided as measures of resistance to mastitis. The objective of this study was to estimate the effect of BoLA class II DQ genes on the breeding value for SCC, in comparison to the effect observed previously on the breeding value for clinical mastitis (Lundén et al. 1990).

MATERIAL AND METHODS

The analysis included 196 AI bulls from 41 sires of the Swedish Red and White breed. The bulls were sampled from the yearly batches of bulls undergoing progeny testing. Semen from the bulls were used for insemination of randomly chosen cows within the regions of two AI societies. Since 1984, all veterinary treatments for clinical mastitis are registered by the Swedish Association for Livestock Breeding and Production (SHS). Disease data, recorded from 10 days before the onset of first lactation to 150 days after calving, are used for estimation of bull breeding values for clinical mastitis. Recently, it has been

decided also to provide bull breeding values for SCC in milk. The underlying data consists of monthly records of bucket somatic cell counts, registered simultaneously with data on milk production in the milk recording scheme. Since the previous analysis, a few of the bulls have been selected for breeding based on their results in the progeny test. Thus, the number of daughters per bull has increased to between 104 and 5250. However, there were only 11 bulls with more than 1000 daughters, whereby the median number amounted to 168 daughters per bull. The breeding values were taken from the routine evaluation system adapted at SHS. A BLUP procedure was used and the model included the effect of sire together with the relationship matrix and fixed effects of herd-year-season, month and age of calving, and breed of dam (NBC, 1987).

The BoLA class II type of the bulls was determined by use of restriction fragment lenght polymorphism (RFLP). Genomic DNA was isolated from doses of frozen semen, and Southern blot analysis was carried out using human probes and two restriction enzymes, TaqI and PvuII. These procedures and the interpretations and nomenclature of DQ RFLPs, have been described previously (Andersson et al. 1986a; 1988; Sigurdardóttir et al. 1988).

The effect of DQ haplotypes on the breeding values for clinical mastitis and SCC, was studied using least-square analysis. A multiple regression model in accordance with Østergård et al. (1989), was used as follows:

$$\text{bull B.V.} = \text{sire B.V.} + \text{BoLA} + e$$

where

- bull B.V. = bull breeding value for clinical mastitis or SCC
- sire B.V. = regression of a bull's breeding value for clinical mastitis or SCC on the breeding value of his sire for the corresponding trait
- BoLA = regression of a bull's breeding value for clinical mastitis or SCC on his number of copies (0,1 or 2) of each DQ haplotype
- e = residual random term

In order to remove dependencies in the data, a restriction was imposed on the regression coefficients so that they sum to zero. In this model, the separate effects of the various DQ haplotypes were simultaneously estimated and tested for significance. All effects in the model, except the residuals, were considered as fixed. It should be noted that this model tests exclusively for additive effects of the various MHC alleles present in the bulls, since the DQ typings were made on the breeding bulls while the mastitis data were collected on their daughters. The effects of the genetic background was considered by the regression of the sire breeding value. Then even bulls with no half sibs contributes to the solution and the effective number of observations increased, compared to a model with sire as a classified effect. The GLM procedure of the Statistical Analysis System was used for the statistical analyses (SAS Institute Inc., 1985). The statistical model and the animal material is described in detail by Lundén et al. (1990).

RESULTS

The statistical analyses showed that bulls carrying the DQ^{1A} haplotype had significantly lower breeding values for clinical mastitis than bulls with other DQ haplotypes (Table 1). None of the DQ haplotypes showed any significant effect on the breeding value for SCC. For DQ^{3}, there is a tendency towards an unfavourable relationship with SCC. The frequency of DQ^{3} is, however, low in this material, which makes it difficult to discriminate between a real effect of DQ^{3} and a spurious effect due to sampling errors. DQ^{1A}, however, is a more frequent

haplotype, present in most half-sib families. For comparison, a model was tested in which the sire effect was treated as a fixed class variable. This model gave results comparable to the results from the covariate model.

Table 1 DQ haplotype frequencies and coefficients of regression (with SE and P-values) for DQ haplotypes, on breeding values for clinical mastitis and somatic cell counts

DQ haplotype	Frequency	Clinical mastitis	P-value	Somatic cell counts	P-value
1A	0.16	-1.11 ± 0.5	0.03 *	-0.54 ± 0.8	0.47
1B	0.10	0.10 ± 0.5	0.85	0.42 ± 0.8	0.61
2	0.19	0.38 ± 0.4	0.40	0.38 ± 0.7	0.57
3	0.03	-0.59 ± 1.0	0.54	-2.74 ± 1.5	0.06(*)
4	0.09	-0.01 ± 0.6	0.99	-0.01 ± 0.9	0.99
5	0.07	0.05 ± 0.6	0.94	0.66 ± 0.9	0.48
6	0.08	0.63 ± 0.6	0.31	1.09 ± 0.9	0.24
7	0.04	-0.23 ± 0.8	0.78	-0.90 ± 1.2	0.47
8	0.03	-0.13 ± 0.9	0.89	0.40 ± 1.4	0.78
9	0.12	-0.07 ± 0.5	0.90	-0.97 ± 0.8	0.24
10	0.04	0.46 ± 0.9	0.60	1.89 ± 1.3	0.16
rare *	0.05	0.38 ± 0.7	0.58	0.33 ± 1.0	0.75

* DQ haplotypes assigned "rare" have frequencies below 0.03
(*) = $P \leq 0.1$ and * = $P \leq 0.05$

DISCUSSION

In the Nordic countries there are unique opportunities to study various aspects of disease resistance, due to the existence of a recording system of all veterinary treatments on dairy cows. In addition, SCC on individual cows are registered in the milk recording scheme. The data obtained are used for construction of breeding values, estimated with high accuracy on large progeny groups. Although SCC is an indirect measure of mastitis, heritability estimates are generally higher for a continuous trait like SCC than heritability estimates for clinical mastitis, treated as an all-or-none trait (for review see Emanuelson, 1988). Breeding values for SCC can therefore be used in selection for improved resistance to mastitis. When studying the influence of genetic markers on quantitative traits, the use of breeding values as the independent variable will reduce the number of animals that need to be typed. This is an advantage especially when the RFLP technic, which is rather costly and laborious, is used for typing. However, non-additive effects cannot be studied by this approach.

Although the bull breeding values have been continuously updated since the previous analysis (Lundén et al. 1990), the results in the present study regarding the negative effect of BoLA DQ^{1A} on clinical mastitis, is in agreement with the former analysis. However, the practical significance of this finding appears limited, since the variation in bull breeding values for clinical mastitis due to DQ^{1A} has been shown to be small (Lundén, et al. 1990). The non-significant effect of DQ^{1A} on SCC, suggests that the observed association, if not a spurious one, primarily concerns clinically manifested mastitis. It is clear that breeding values for clinical mastitis and SCC do not measure entirely the same trait, as the genetic correlation between the two traits varies around 0.6 (Emanuelson et al. 1988). While recordings on veterinary treatments mainly reflect the frequency of clinical mastitis, high scores for SCC account for both clinical and subclinical forms of mastitis. It has been shown that less aggressive

pathogens, frequently causing subclinical mastitis with high SCC scores, only infrequently cause clinical mastitis, which results in many "false positives". There are even indications on a protective effect of less aggressive bacteria towards some of the more pathogenic ones (Holmberg, 1986). Also false negatives are likely to occur, as the SCC level is known to fluctuate considerably during the subclinical phase of mastitis. When the time span between two SCC recordings exceeds one month, which is the case during summer in Sweden, a clinical mastitis will have time to both develop and be cured without necessarily result in high SCC scores.

The results presented here point towards a significant effect of BoLA DQ^{1A} on susceptibility to mastitis and, furthermore, that this effect mainly concerns clinically manifested mastitis. However, the results need to be confirmed on independent materials. The significance of this observation is difficult to assess before more is known about the causal relationship between BoLA DQ^{1A} and susceptibility to clinical mastitis. One possible explanation might be that the immune response in DQ^{1A}-positive individuals is efficient towards less pathogenic bacteria, while the response towards more aggressive pathogens is inadequate. Therefore, a future object would be to compare the effect of DQ^{1A} on more aggressive pathogens causing clinical mastitis, with the effect on less aggressive pathogens associated mainly with subclinical symptoms.

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