Effects of Casein Haplotypes on Milk Production Traits in Italian Holstein and Brown Swiss Cattle

P. J. Boettcher,¹ A. Caroli,² A. Stella,³ S. Chessa,⁴ E. Budelli,³ F. Canavesi,⁵
S. Ghioldi,⁶ and G. Pagnacco⁴

¹Institute of Agricultural Biology and Biotechnology, National Research Council, Segrate 20090, Italy

²Dipartimento di Sanità e Benessere degli Animali, Università di Bari, Valenzano 70010 Italy

³Centro Ricerche e Studi Agroalimentari, Fondazione Parco Tecnologico Padano, Segrate 20090, Italy

⁴Dipartimento di Scienze e Tecnologie Veterinarie per la Sicurezza Alimentare,
Università degli Studi di Milano, Italy

⁵Associazione Nazionale Allevatori Frisone Italiana, Cremona 26100, Italy

⁶Associazione Nazionale Allevatori Razza Bruna Italiana, Bussolengo 37012, Italy

ABSTRACT

The objective of this study was to estimate the effects of different haplotypes of the casein genes on milk production traits in Italian dairy cattle. Traits of interest were yields of milk, fat, and protein, and percentages of fat and protein in milk. The data included 728 multiparous records from 347 Holsteins and 773 records from 298 Brown Swiss cows. Records were preadjusted for effects of age and parity, season of calving, and region, and expressed as deviations from herd-mate averages. Twenty half-sib families were represented in each breed. Haplotype probabilities were estimated for each animal and phenotypes were regressed on these probabilities. Nine haplotypes were observed in Holsteins and 17 were identified among the Brown Swiss. For Holsteins, significant effects were observed for protein percentage, with some indication of an effect for fat percentage. For the Brown Swiss, effects of haplotypes were significant for milk yield and fat and protein percentages. Effects were strongest for protein percentage. Correlation coefficients of solutions across breeds tended to be strong and positive, indicating that the same haplotypes had similar estimated effects in the 2 breeds. Although the data were limited (<350 cows in each study), this latter result may suggest that genes in the casein complex itself are responsible for the effects observed, rather than loci that are physically linked on either side of the casein cluster.

(Key words: haplotype, casein, cattle, milk production)

INTRODUCTION

Much evidence has been presented that demonstrates effects of genes on cattle chromosome 6 on milk produc-

tion traits of dairy cattle. Multiple genome scans have reported a high probability of segregating QTL in this region that affect milk production traits (e.g., Van Tas-sell et al., 2000; Olsen et al., 2002; Viitala et al., 2003). The genes that encode milk CN proteins are known to be located on this chromosome (Ferretti et al., 1990; Threadgill and Womack, 1990). Candidate gene studies have examined relationships between different alleles of the various CN genes. Two approaches have been taken. Some studies have looked at associations between phenotypes of cows and their CN genotypes (e.g., Bovenhuis et al., 1992; Ojala et al., 1997; Ikonen et al., 1999), whereas others have looked at associations between EBV of bulls and their respective genotypes (Ron et al., 1994; Sabour et al., 1996). These studies have found some statistically significant associations between different CN alleles and milk production traits.

Results of studies considering the effects of single protein genes have not been consistent. Some investigations have found a positive effect for the B allele of the κ -CN locus (e.g., Ng-Kwai-Hang et al., 1986; Cowan et al., 1992), but other studies have failed to corroborate this result (Ron et al., 1994; Sabour et al., 1996). This result seems to suggest that the significant effects observed in some studies were due not only to the κ -CN gene, but also possibly to other genes or combination of genes physically linked to this locus. Genes that encode α_{S1} -CN and β -CN are also located on chromosome 6, within a region of about 200 kb that includes κ -CN (Ferretti et al., 1990; Threadgill and Womack, 1990). This closeness in physical location makes it difficult to separate the effects of different CN genes (Lien et al., 1995). For this reason, several investigators have taken a different approach for estimating effects associated with different combinations of the CN alleles. Instead of analyzing effects of single alleles, these studies estimated effects of haplotypes defined by the CN genes (e.g., Braunschweig et al., 2000; Ikonen et al., 2001) and, in some cases, by other sites of polymorphism

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Corresponding author: Paul Boettcher; e-mail: boettch@ibba.cnr.it.

within the area of chromosome 6 linked to the CN loci (Lien et al., 1995). Various significant effects have been observed in these studies, particularly for protein content in milk.

The commonly used genotyping procedures currently applied in molecular genetic studies yield only information about the 2 alleles present at a given locus of diploid individuals. When multiple loci are genotyped, haplotypes are not known, because no information is produced regarding the linkage phase of the alleles at the different loci. Definition and assignment of haplotypes must be done in a separate step, using information about genotypes of individuals within the same family or the population to reconstruct and deduce the most probable haplotype for each individual. One common approach taken for analyses of haplotype effects (and the approach taken in the previously mentioned studies on CN haplotypes) has been to determine the most likely haplotype configuration for each individual and assume that this haplotype assignment is known without error when subsequent statistical analyses are performed. One problem with this approach is that haplotype configurations are usually impossible to determine unambiguously for some individuals. Therefore, another option for such analyses would be to estimate the probability of each haplotype configuration for each individual and then to regress phenotypes on the respective probabilities for each haplotype. Such an approach would help account for the uncertainty of haplotype reconstruction and could yield greater precision in the analysis.

A question of interest in studies on CN haplotypes is whether the effects observed are due to differences among genes within the CN complex or to genes linked physically on chromosome 6. Finding similar effects of the same haplotypes in different breeds would provide some evidence that the effects observed were due to the direct effects of the CN loci or to DNA polymorphisms within the casein complex. In contrast, differences among breeds would tend to rule out this conclusion, suggesting that differences were also associated with other factors, such as direct effects of other genes linked to the CN loci or interaction with loci in other regions of the genome. The logic behind this hypothesis is that the casein complex is rather short at 200 kb and thus may be subject to little recombination.

The objective of this study was to estimate the effects of CN haplotypes on milk production traits in 2 breeds, Italian Holstein and Brown Swiss, and to compare effects of the same haplotypes in the 2 breeds.

MATERIALS AND METHODS

Effects of haplotypes were estimated in 2 steps, first determining the probability of each haplotype for each

individual based on genotypic information and then regressing phenotypes on a function of these probabilities. Genotypes for α_{S1} -, β -, and κ -CN were available for 352 Italian Holstein and 311 Brown Swiss, based on milk samples collected in 2001. Genotypes had been determined by isoelectric focusing analysis of individual milk samples according to Erhardt et al. (1998). Twenty different sires were represented in each breed. The number of daughters per sire ranged from 8 to 28 for Holsteins and from 9 to 22 for Brown Swiss. Haplotypes were reconstructed separately for each breed, using the Monte Carlo based method of Boettcher et al. (2004). This procedure involved 2 steps. In the first step, haplotype probabilities of the sires were determined, conditional upon genotypes of the offspring and allelic frequencies in the general population. Briefly, for each sire, all possible haplotype configurations were identified based on offspring genotypes. Then, for each plausible haplotype combination for that sire, random gametes were sampled for the offspring that were consistent with their respective genotypes. The complementary dam gametes were then determined and the probability of receiving this combination of sire and dam gametes was determined based on population haplotype frequencies, recombination rates, and probability theory. This process was repeated many times for each plausible sire haplotype combination and summed together within each combination to obtain a relative probability for each. Relative probabilities were converted to absolute probabilities by standardizing by the sum of all relative probabilities. In the second step, the haplotype probabilities of offspring were then directly calculated conditional upon these sire haplotype frequencies. These 2 steps were alternated iteratively until estimated population frequencies within the breed of interest converged to stable values. The final result was a set of estimated haplotype probabilities for each animal, expressed as the expected number of copies of each haplotype carried by each animal.

Phenotypic records for 305-d yields of milk, fat, and protein, and percentages of fat and protein were obtained from the Italian Holstein (ANAFI, Cremona, Italy) and Brown Swiss (ANARB, Bussolengo, Italy) Associations. Data had been preadjusted for age, parity, month of calving, and region effects and deviated from contemporary group means. Preadjustment of records was expected to be much more precise than directly accounting for the various systematic nongenetic effects in the model. Adjustments had been made based on factors calculated using the national databases for each breed, which include hundreds of thousands of records, vs. only a few hundred for this study. For a similar reason, using deviations from contemporary groups in the national databases was expected to be superior to

including contemporary groups in the eventual statistical model. Cattle were selected for the project based on sire, rather than herd, and most cows had many fewer herdmates in the study than present in the national databases. Holstein cows were from 51 different herds and Brown Swiss were from 77. Phenotypic data were not available for all cattle with CN genotypes, and some cows had multiple records. After keeping only those records from cattle with both types of information, the final datasets included 728 records from 347 Holstein cows and 773 records from 298 Brown Swiss cows. The Italian national evaluation for Holsteins considers only the first 3 lactations, whereas all records are eligible for the Brown Swiss, which explains why the average number of records per cow was greater for Brown Swiss. Among Holsteins, 93 cows had only a single record, and 129 had 3 records. For Brown Swiss, 77 cows had only first parity information, and 134 had >2 records. Breeds were analyzed separately.

The goal of the analysis was to estimate haplotype effects by regressing phenotypes on haplotype probabilities (expressed as expected numbers of copies of each haplotype). Because these expected values summed to exactly 2.0 for each individual, linear dependencies existed among haplotype probabilities. Thus, a standard regression approach would not have allowed for the estimation of both an overall intercept and a separate regression coefficient for each haplotype. Therefore, before the statistical analysis, the overall mean was subtracted from the record for each trait, forcing an implicit restriction that the sum of haplotype effects (weighted for individual probabilities) in the population was equal to zero. Then regression was applied without including an intercept in the model, allowing for no explicit restrictions on the fixed effects and the estimation of a regression coefficient for each haplotype. Rare haplotypes (frequency <0.005) were grouped together into a single common effect.

The model used for the statistical analyses was:

$$y_{ijk} = \sum_{a=1,h} \beta_a p_{a:ij} + s_i + c_{ij} + e_{ijk}, \quad [1]$$

where y_{ijk} was the k th phenotypic record (preadjusted effects of age, parity, herd-year-season and deviated from the population mean) for the j th daughter of the i th sire, h is the total number of haplotypes evaluated, β_a is the regression coefficient for the effect of a single haplotype a , $p_{a:ij}$ is the probability that daughter j of sire i carried haplotype a , s_i is the random effect of sire i , c_{ij} is the random effect of the j th daughter of sire i (nested within sire i), and e_{ijk} is the random residual. A sire model was chosen rather than an animal model because the procedure for selection of animals resulted in very few close maternal genetic relationships (i.e.,

mother-to-daughter or maternal half-sibs). Thus, an expectedly small amount of statistical precision was sacrificed for the increased operational simplicity of the sire model. Equation 1 was solved using maximum-likelihood and the MIXED procedure for SAS software (SAS Institute, Inc., Cary, NC). Variances for sire, cow, and residual effects were estimated simultaneously with the estimation of fixed effects.

The regression coefficients β_a from equation 1 allow one to calculate the expected difference in a given trait between 2 animals with different casein haplotypes. In the hypothetical situation in which 2 animals differed at only one haplotype, the expected difference in a given trait would be the difference between the solutions of the different haplotypes that the 2 animals carry. For example, consider 2 cows that are alike in all ways (including one of the 2 haplotypes) except that one cow carries hypothetical haplotype X and the other carries Y. Assuming that the respective regression coefficients for these 2 haplotypes were +100 and -200, the milk yield of the first cow would be expected to exceed that of the second by 300 kg.

To determine the statistical significance of the haplotype effects, we tested the null hypothesis that all regression coefficients were equal to zero. In addition, P values of the estimates of the effects of each haplotype were also obtained. To determine if the estimates of haplotype effects were similar across breeds, simple Pearson correlations were calculated across breeds for each trait, using solutions for the haplotypes that were present in both breeds. Only a small number of haplotypes were present in both breeds, thus the precise values of correlation coefficients between solutions were clearly not expected to have the same meaning as a correlation coefficient calculated on a very high number of observations. For example, such correlations could not be converted to meaningful regression coefficients to estimate the change in one variable associated with a unit change in the other variable. However, high and positive correlations were still expected to indicate similarity of effects across breeds. In addition, the correlations were not likely to be distributed with a normal distribution under the null hypothesis. Therefore, a permutation test was used to test for significance of the resulting correlation coefficients.

Under the null hypothesis of no similarity in solutions for the same haplotypes across breeds, one would expect the correlation of solutions across breeds to be near zero and the way in which individual haplotype solutions were paired across breeds to calculate a correlation coefficient should have no particular relationship with the magnitude of the correlation. Thus, to perform the permutation test on the correlations observed for the N haplotypes in common across breeds, we calcu-

Table 1. Means¹ and standard deviations of the traits for each breed.

Trait	Holstein (n = 728 ²)		Brown Swiss (n = 773)	
	Mean	SD	Mean	SD
Milk, kg	509	1294	148	754
Fat, kg	17	56	8	30
Protein, kg	19	37	6	24
Fat, %	0.00	0.40	0.04	0.26
Protein, %	0.04	0.18	0.01	0.16

¹Reported values are means of deviations from herdmates.

²From 347 Holstein and 298 Brown Swiss cows.

lated the correlation coefficient for each of the $N!$ possible ways of pairing the N different solutions for each trait across breeds. Then, for each trait, the P value was estimated as the proportion of pairing schemes that yielded greater or equal correlation coefficients than that observed when solutions were paired according to the haplotypes.

RESULTS AND DISCUSSION

Phenotypic Data

Means of deviated records for yield traits were greater than zero for both breeds, suggesting that the cattle evaluated in this study were better than average producers in their respective herds (Table 1). This result was not unexpected, given that the cattle used for this study were from sires that were used heavily enough to have obtained numerous daughters in different herds. The standard deviations of yield traits were greater for the Holsteins than for the Brown Swiss, which was also expected, given that Holsteins had greater mean milk yield (8815 vs. 6429 kg) and variation in yield tends to be positively associated with mean yield (Visscher et al., 1991). Overall means for fat and protein yield were 314 and 299 kg, respectively, for Holsteins, and 244 and 221 kg for Brown Swiss.

Haplotype Frequencies

Two alleles (B and C) were present for α_{s1} -CN in the sample of Holstein cattle. Four alleles (A^1 , A^2 , A^3 , and B) were present for β -CN, and 3 κ -CN alleles (A, B, and E) were observed. Among the Brown Swiss, an additional F allele was observed for α_{s1} -CN and some cattle carried the C allele of κ -CN, whereas the E allele of κ -CN was not present. Fifteen different genotypes were observed among the Holsteins, with (α_{s1} , β , κ -CN) BBA¹A²AA (26%), BBA²A²AA (24%), and BBA¹A²AE (12%) being the most common. Brown Swiss cows had 33 different genotypes, with the 3 most common being BBA²A²BB (28%), BBA²BAB (12%), and BBA²A²AB

(9%). Based on the distributions of alleles, a maximum of 24 ($2 \times 4 \times 3$) haplotypes were possible among Holsteins and 36 ($3 \times 4 \times 3$) were possible for Brown Swiss. Following haplotype reconstruction, 9 different plausible haplotypes were observed among the Holsteins and 17 were present for the Brown Swiss. Estimated haplotype frequencies of the most common (frequency > 0.005) are shown in Table 2 for Holsteins and Table 3 for Brown Swiss. The most common haplotype among Holsteins was BA²A (α_{s1} - β - κ), with an estimated frequency of 0.48. More than 75% of the haplotypes present were either BA²A or BA¹A. The BA²B haplotype was the most common (0.50) among the Brown Swiss. The frequency of this haplotype was only about 5% among the Holsteins (Table 2). The next 2 most common haplotypes, BA¹A and BA²A (Table 3), each had a frequency of about 10%. Several haplotypes had estimated frequencies <0.005 for the Brown Swiss. Some of these rare haplotypes may not have actually existed in the population, but were among the plausible haplotypes for some individuals as identified by the reconstruction program.

Haplotype Effects

Tables 2 and 3 have estimates of haplotype effects and results of significance tests for Holsteins and Brown Swiss, respectively. Significance tests were based on nominal values of significance. The effects of haplotypes were significant ($P < 0.05$) only for protein percentage in Holsteins (Table 2). Some evidence of an effect for fat percentage ($P < 0.10$) was also observed. This result is consistent with previous scans of chromosome 6 (Kühn et al., 1999; Velmala et al., 1999) and estimates of haplotypic effects for this region in other breeds (e.g., Ikonen et al., 2001). For the Brown Swiss (Table 3), haplotype effects were highly significant ($P < 0.001$) for both fat and protein percentage. In contrast to the results observed in Holsteins, milk yield was also affected by differences in the CN haplotypes ($P = 0.0091$).

In Holsteins, the BA¹B haplotype was associated with increased percentages of fat (0.16) and protein (0.09). Ikonen et al. (2001) reported a positive effect for this haplotype on these traits in Finnish Ayrshires. The BBA haplotype had the unusual effect of increasing fat percentage (0.11) and decreasing protein percentage (−0.08), whereas the CA³A haplotype had opposite effects on the same traits. However, both of these haplotypes were rare and the estimates of their effects had high standard errors and were not significant statistically ($P > 0.05$).

Similar to Holsteins, the BA¹B haplotype was associated with increased fat and protein percentages ($P < 0.01$) in Brown Swiss (Table 3). This haplotype also had

Table 2. Estimates of haplotype frequencies and effects (SE in parentheses) on milk production traits in Italian Holstein cows (n = 347).

Haplotype	Frequency ¹	Milk	Fat	Protein	Fat	Protein
($\alpha_{S1}-\beta-\kappa$)		(kg)			(%)	
BA ¹ A	0.28	86 (80)	2.8 (3.2)	2.7 (2.3)	-0.01 (0.026)	-0.00 (0.01)
BA ¹ B	0.04	-218 (190)	4.4 (8.3)	-0.3 (5.4)	0.16 (0.059)**	0.09 (0.03)**
BA ¹ E	0.06	-71 (170)	1.5 (7.4)	-2.2 (4.8)	0.06 (0.053)	0.00 (0.02)
BA ² A	0.48	36 (60)	-0.1 (2.7)	0.3 (1.8)	-0.01 (0.02)	-0.01 (0.01)
BA ² B	0.05	52 (190)	-5.3 (8.3)	6.1 (5.4)	-0.08 (0.06)	0.05 (0.03)†
BA ² E	0.02	-157 (337)	4.0 (14.5)	-7.7 (9.5)	0.08 (0.10)	-0.05 (0.05)
BBA	<0.01	325 (433)	25.7 (18.6)	5.0 (12.2)	0.13 (0.12)	-0.08 (0.06)
BBB	0.06	-85 (148)	-2.2 (6.5)	-3.2 (4.2)	0.01 (0.05)	-0.05 (0.05)
CA ³ A	<0.01	-290 (526)	-24.9 (23)	1.4 (15.8)	-0.16 (0.16)	0.122 (0.07)†
Overall <i>P</i>	...	0.90	0.84	0.84	0.09†	0.01**

†*P* ≤ 0.10.**P* ≤ 0.05.***P* ≤ 0.01.¹Other rarer haplotypes accounted for <1% of the population.

a negative effect on milk yield (*P* < 0.05), which was consistent with its effect in Holsteins (Table 2), although the effect in Holsteins was not significant. The CA²B haplotype had effects similar to BA¹B, in that it was associated with significantly decreased yield and increased concentration of protein. Three other haplotypes (BA²A, BBA, and BBB) had significant (*P* < 0.05) effects on protein percentage. In general, among haplotypes differing only at the κ -CN locus, those haplotypes with the B allele had positive effects on protein percentage relative to the corresponding haplotype with the A allele, which was consistent with previous studies that had found differences between κ -CN genotypes (Ng-Kwai-Hang et al., 1986; Cowan et al., 1992; Ikonen et al., 2001).

Comparing results across breeds, one similarity was that the same traits – protein percentage in particular,

and fat percentage to a lesser degree – were affected most strongly by differences in CN haplotypes. As mentioned previously, haplotype BA¹B was associated with significant increases in fat and protein percentages in both breeds. Ikonen et al. (2001) observed similar effects for this haplotype in Finnish Ayrshires, and Caroli et al. (2004) reported a positive effect of this haplotype on protein percentage in the local Reggiana cattle breed of Italy.

Six haplotypes (BA¹A, BA¹B, BA²A, BA²B, BBA, and BBB) were present in both breeds. Table 4 has correlation coefficients across breeds for haplotype effects for each trait. Correlations between haplotype solutions were positive for all traits and above 0.50 for all traits except protein yield. The correlation for milk yield was particularly high (0.81). According to the permutation test procedure, only 5 (<1%) of the 720 possible pairing

Table 3. Estimates of haplotype frequencies and effects (SE in parentheses) on milk production traits in Italian Brown Swiss cows (n = 298).

Haplotype	Frequency ¹	Milk	Fat	Protein	Fat content	Protein content
($\alpha_{S1}-\beta-\kappa$)		(kg)			(%)	
BA ¹ A	0.10	34 (190)	0.4 (7.7)	-2.0 (6.2)	-0.02 (0.06)	-0.05 (0.04)
BA ¹ B	0.01	-397 (183)*	3.2 (7.3)	-5.2 (5.6)	0.27 (0.06)***	0.11 (0.04)**
BA ² A	0.11	91 (68)	2.2 (2.6)	-0.5 (2.1)	-0.02 (0.02)	-0.06 (0.02)***
BA ² B	0.50	31 (42)	-0.6 (1.6)	1.1 (1.2)	-0.02 (0.01)†	-0.00 (0.01)
BBA	0.11	113 (72)	3.8 (2.8)	0.7 (2.2)	-0.01 (0.02)	-0.04 (0.02)**
BBB	0.07	-36 (75)	2.2 (2.6)	2.8 (2.4)	0.05 (0.03)†	0.06 (0.02)**
CA ² A	0.02	-252 (130)	-6.9 (5.2)	-8.2 (4.1)*	0.04 (0.04)	-0.01 (0.02)
CA ² B	0.05	-248 (98)*	-6.1 (3.9)	-2.8 (3.1)	0.05 (0.03)	0.08 (0.02)***
FA ² B	0.01	-1525 (1174)	-75.7 (47.6)	-46.8 (38.1)	-0.27 (0.40)	0.06 (0.23)
Overall <i>P</i>	...	0.01**	0.18	0.28	<0.001***	<0.0001***

†*P* ≤ 0.10.**P* ≤ 0.05.***P* ≤ 0.01.****P* ≤ 0.001.¹Other rare haplotypes accounted for <2% of the population.

Table 4. Correlations of haplotype effects across breeds for each trait.

Trait	Correlation	P-value ¹
Milk, kg	0.81	0.01**
Fat, kg	0.69	0.03*
Protein, kg	0.06	0.44
Fat, %	0.68	0.05*
Protein, %	0.54	0.13

* $P \leq 0.05$.** $P \leq 0.01$.¹Based on a permutation test.

schemes yielded higher correlation coefficients. In addition, fewer than 5% of the permutations of paired solutions yielded higher correlations for fat yield and fat percentage.

Because numbers of shared haplotypes were low and because some haplotypes were rather rare in at least one of the breeds (e.g., BBA in Holsteins), additional evidence of similarity of haplotype effects across breeds was sought by comparing estimates of haplotype effects from this study to those obtained in the study of Ikonen et al. (2001) in Finnish Ayrshires. Four haplotypes (BA₁A, BA₁B, BA₂A, and BA₂B) were shared across 3 populations (Italian Holstein and Brown Swiss). Correlations were calculated between the solutions obtained in this study and the estimated effects of a single haplotype reported by Ikonen et al. (2001) for milk and protein yields, and fat and protein percentages (fat yield was not reported for the Finnish Ayrshires). Correlations of estimated haplotype effects for Italian Holstein and Brown Swiss with those for Finnish Ayrshires were again consistently very highly positive for all traits examined. Specifically, correlations for Holsteins and Brown Swiss, respectively, were 0.58 and 0.72 for milk yield, 0.84 and 0.62 for protein yield, 0.83 and 0.76 for fat percentage, and 0.87 and 0.88 for protein percentage. Due to the small number (4) of shared haplotypes, none of these correlations were statistically significant in their own right; however, the consistent pattern of highly positive correlations across breeds for all traits seems to provide evidence of real and similar effects of the CN region across breeds. This hypothesis is strengthened by the fact that the results in Finnish Ayrshires were based on records from nearly 17,000 cattle.

Although the number of animals evaluated in this study was rather low (347 Holsteins and 298 Brown Swiss for a total of slightly less than 650 cattle), the positive significance tests across breeds for multiple traits seem to suggest that genes within or near the CN region have effects on milk production traits. Assuming these effects are real, the high correlations across breeds may indicate that the CN protein sequences

themselves or DNA polymorphisms within the CN complex are responsible for the effects on the various traits, rather than other genes linked to these loci. If effects were due to linked genes, similar haplotype solutions would have been observed only if the linkage phase with the CN alleles was the same across breeds, which seems unlikely. Interactions of CN loci with other polymorphisms in the CN complex may be present, which could help explain why haplotype effects ranked similarly in both breeds but were more distinct in the Brown Swiss than in Holsteins. Sites of polymorphism within noncoding regions within the CN complex have been recently identified. Damiani et al. (2000b) described a polymorphism within the short interspersed nucleotide element Bov-A2 in the second intron of κ -CN. This polymorphism was found to be in linkage disequilibrium with the κ -CN protein variants (Damiani et al., 2001), and had statistically significant associations with several milk production traits (Damiani et al., 2000a). More recently, polymorphisms of the α_{s1} -CN promoter were found have significant associations with milk protein content (Prinzenberg et al., 2003). Thus, the CN polymorphism has to be considered as a whole complex where expression sequence polymorphisms could help explain the productive implications of the different CN loci and their corresponding haplotypes.

CONCLUSIONS

Statistically significant associations between CN haplotypes and production traits were observed in Italian Holstein and Brown Swiss. The greatest relationships were observed for protein percentage, although milk yield and fat percentage were also significantly associated. The estimated effects of the same haplotypes were similar across breeds, but greater in magnitude for the Brown Swiss. This similarity in effects across breeds may suggest real influences of the actual CN haplotypes on the traits evaluated, which may have been due to positive effects of the B allele of κ -CN. However, some caution must be used when interpreting these results, given that they were based on records from <350 animals per breed and only 6 haplotypes were present in both breeds. From a biological point of view, further investigation is required to confirm these results and to obtain more details about the precise polymorphisms that could be responsible for associations related to the CN complex. If observed effects are real, such work could increase the value of the CN complex for use in marker-assisted selection, which remains questionable based on the current work, inasmuch as the haplotypes that improved fat and protein percentage were also associated with decreased milk yield and only small effects on yield of fat and protein.

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