Quantitative Trait Loci Affecting Fertility and Calving Traits in Swedish Dairy Cattle

M. Holmberg¹ and L. Andersson-Eklund

Department of Animal Breeding and Genetics, Swedish University of Agricultural Sciences, Box 7023, 75007 Uppsala, Sweden

ABSTRACT

Impaired fertility is the main reason for involuntary culling of dairy cows in Sweden. The objective of this study was to map quantitative trait loci (QTL) influencing fertility and calving traits in the Swedish dairy cattle population. The traits analyzed were number of inseminations, 56-d nonreturn rate, interval from calving to first insemination, fertility treatments, heat intensity score, stillbirth, and calving performance. A genome scan covering 20 bovine chromosomes was performed using 145 microsatellite markers. The mapping population consisted of 10 sires and their 417 sons in a granddaughter design. Nine of the sires were of the Swedish Red Breed, and one was a Swedish Holstein. Least squares regression was used to map loci affecting the analyzed traits, and permutation tests were used to set significance thresholds. Cofactors were used in the analyses of individual chromosomes to adjust for QTL found on other chromosomes. The use of cofactors increased both the number of QTL found and the significance level. In the initial analysis, we found 13 suggestive QTL that were mapped to chromosomes 6, 7, 9, 11, 13, 15, 20, and 29. When cofactors were included, 30 QTL were detected on chromosomes 1, 3, 4, 18, 19, 22, and 25, in addition to the 8 previously mentioned chromosomes. Some of the results from the cofactor analysis may be false positives and require further validation. In conclusion, we were able to map several QTL affecting fertility and calving traits in Swedish dairy cattle.

Key words: quantitative trait loci, fertility, calving, dairy cattle

INTRODUCTION

Fertility and calving traits are of significant economic importance in dairy cattle production. Poor reproductive performance is the most common reason for culling and today 26% of all disposals in the main dairy breeds

in Sweden are due to impaired fertility (Swedish Dairy Association, 2004). The consequences of low fertility include additional inseminations, higher veterinary costs, increased culling rate, and higher replacement costs. Calving performance and calf viability are important traits not only for economic reasons but also for animal welfare.

Reproduction traits are quantitative traits because they are regulated by several genes and are largely influenced by the environment. These traits have a low heritability, usually below 5% (Roxstrom et al., 2001; Wall et al., 2003). However, the low heritability is due to a large phenotypic variation and the genetic variation is still quite large (Philipsson, 1981; Roxstrom, 2001; Wall et al., 2003). It is also well known that the genetic correlation between fertility and production is generally unfavorable (Hoekstra et al., 1994; Roxstrom et al., 2001). The large environmental influence and the negative genetic correlation make it costly and demanding to achieve a significant genetic improvement in reproduction traits by traditional selection based on breeding values.

Molecular techniques have made it possible to locate loci involved in the expression of a quantitative trait by combining information on genetic markers and phenotypic information on a trait. A QTL is defined as a chromosomal segment with an effect on a quantitative trait. A few studies have described QTL for reproduction traits in different populations (Schrooten et al., 2000; Kuhn et al., 2003; Schulman et al., 2003). Marker-assisted selection is expected to be beneficial in selection for sex-limited traits or traits that are expressed late in life. Marker-assisted selection could also be used to select for specific QTL that have positive effects on reproduction without antagonistic effects on production. Thus, marker-assisted selection may be useful if we can identify QTL accounting for a significant proportion of the genetic variation in fertility.

In a previous study, the same animal material was used in a partial genome scan of 17 chromosomes to detect QTL for health traits (Holmberg and Andersson-Eklund, 2004). The objective of the present study was to map QTL contributing to the genetic variation in fertility and calving traits in the Swedish dairy cattle population.

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¹Corresponding author: mia.holmberg@hgen.slu.se

MATERIALS AND METHODS

Resource Population and Marker Data

The mapping population was the same as in the study described by Holmberg and Andersson-Eklund (2004). Ten paternal half-sib families were included: 9 of the Swedish Red breed, and 1 of the Swedish Holstein breed. The total number of genotyped bulls was 417 and the number of sons per grandsire ranged from 21 to 58 with a mean of 42. Semen samples from all bulls for DNA extraction were obtained from the Swedish breeding company, Svensk Avel.

Three chromosomes [*Bos taurus* autosomes (BTA) 7, 10, and 20] were added to the previously described granddaughter design (Holmberg and Andersson-Eklund, 2004). In addition to the new markers on BTA 7, 10, and 20, 1 microsatellite marker (MS) was added to each of BTA9 and BTA18, and 3 MS to BTA11. The new MS were selected from the Meat Animal Research Center Web site (<http://www.marc.usda.gov/>). In total, 20 chromosomes were included in the study, and 145 genetic markers were genotyped.

The number of genotyped markers per chromosome varied from 4 to 12, and the average number of informative markers (sire heterozygous) per chromosome ranged from 2.5 to 7.4. The mean interval between markers was 20 cM, and ranged from 10 cM on BTA6 to 33 cM on BTA23; detailed information about the linkage groups is given in Table 1. Marker maps were established by using the CRI-MAP program (version 2.4; Green et al., 1990), and the Haldane map function.

Phenotypic Data

Data on 11 traits were analyzed in this study. The fertility traits considered were maternal nonreturn rate (NR) of 56 d in heifers (NR_{56_{heifer}}) and first-lactation cows (NR_{56_{cow}}), number of inseminations in heifers (INS_{heifer}) and first-lactation cows (INS_{cow}), number of fertility treatments (FTR), interval from calving to first insemination (CFI), and heat intensity score (HS). The calving traits were stillbirth (STI) as a direct effect (STI_{dir}) and as a maternal effect (STI_{mat}), and calving performance (CAL) as a direct (CAL_{dir}) and as a maternal effect (CAL_{mat}). A direct effect was defined as calving when the evaluated bull is father of the calf and a maternal effect was defined as when the trait is recorded on daughters of the bull (i.e., the bull is grandfather of the calf).

For NR and number of inseminations, the heifer and cow performance were treated as separate traits. This is because the genetic correlation between fertility traits in the heifer period and the same traits in first-parity cows is only moderately high (0.7; Roxstrom et

Table 1. Linkage groups used in the QTL analysis for reproduction traits in 10 grandsire families

BTA ¹	No. of markers	Length ² (cM)	Average marker interval ² (cM)	Average no. of informative markers ³
1	8	190	27.1	5.1
2	7	175	29.2	5.3
3	11	121	12.1	6.1
4	12	109	9.9	7.4
5	7	133	22.2	4.7
6	6	163	32.6	3.8
7	9	160	20.0	7.2
9	8	163	23.3	4.6
10	8	130	18.6	4.3
11	10	133	14.8	6.1
13	6	95	19.0	3.7
14	6	85	17.0	4.5
15	5	111	27.8	3.1
18	8	129	18.4	5.7
19	7	87	14.5	4.3
20	7	68	11.3	4.7
22	6	124	24.8	4.7
23	6	79	15.8	4.1
25	4	64	21.3	2.5
29	4	89	29.7	2.9
Total	145	2,408	20.5	4.7

¹BTA = *Bos taurus* autosome.

²Haldane mapping function.

³No. of markers that were informative averaged across grandsires and all markers on each chromosome.

al., 2001). Nonreturn rate was based on whether the heifer or cow had a second insemination within 56 d after the first insemination. Nonreturn rate and number of inseminations per service period described the cow's ability to become pregnant after insemination. Fertility treatments were defined as veterinary treatments for fertility disturbances from 10 d before until 150 d after the first calving. The interval from calving to first insemination was measured in number of days, and reflected the cow's ability to recover and to return to cyclicity after calving. The heat intensity score measured the ability of the cow to show estrus. Data on heat score and calving difficulty were generated by the individual farmer who subjectively scored the performance in predefined categories. Stillbirth included calves dead at birth or within 24 h. The calving traits were based on first calvings only and twin calvings were excluded.

The phenotypic data and heritabilities of the traits were obtained from the national genetic evaluation. Daughter group averages (DYD), based on a minimum of 50 daughters per bull and adjusted for systematic environmental effects, were available for all fertility traits except heat score. For the calving traits and heat score, EBV were obtained from the national genetic evaluation, and were used as phenotypic records in the analyses. The median of number of daughters per bull

differed between the traits and varied from 107 to 309 (150 daughters corresponded to reliabilities of EBV or DYD of 0.43 and 0.66 for traits with heritabilities of 0.02 and 0.05, respectively). Estimated heritabilities for the analyzed traits ranged between 0.02 and 0.05.

Statistical Analyses

The QTL analyses were performed for each trait separately with a multimarker regression approach (Knott et al., 1996; Vilkki et al., 1997). At each centimorgan of every chromosome, the phenotypes were regressed on the probability of transmission of alternative paternal QTL alleles to sons. The analysis was nested within families to allow for different linkage phases between markers and QTL between grandsires. The following regression model was applied in analyses both across and within families:

$$Y_{ijk} = \mu + gs_i + b_i X_{ijk} + e_{ijk},$$

where Y_{ijk} is the DYD (or EBV) of son k , of grandsire i , marker genotype j ; μ is the overall mean; gs_i is the effect of grandsire i ; b_i is the regression coefficient within grandsire i ; X_{ijk} is the probability of QTL allele 1 being transmitted from grandsire i , given the pair of informative flanking markers j of son k , and e_{ijk} is the residual effect. The DYD and EBV were weighted for number of effective daughters and heritability of the trait analyzed. The model assumed 1 QTL per chromosome with an additive effect and no interaction.

First, the chromosomes were analyzed individually to identify candidate regions for QTL. To increase the power of the analysis, QTL that reached a chromosome-wise significance of $P < 0.10$ in the across-family analysis were included in the further analyses as cofactors (de Koning et al., 2001). The phenotypic data were adjusted for the effects of the cofactors and the linkage groups were reanalyzed by interval mapping. The analyses were repeated until no new QTL were found and the estimated locations of the identified QTL were stable.

Test statistic used was an F -ratio that was calculated for every position (cM) on all chromosomes. Permutation tests of 10,000 rounds were performed for each trait separately to set chromosome-wise significance levels for analyses within and across families (Churchill and Doerge, 1994). The chromosome-wise P -values obtained from the permutation tests were then used to set genome-wise significance levels by the Bonferroni correction for testing across multiple chromosomes, $P_{\text{genome}} = 1 - (1 - P_{\text{chromosome}})^c$, where c is the total number of cattle autosomes ($c = 29$).

RESULTS

Associations between markers and traits were tested on 20 chromosomes for 11 traits. The order of markers in the linkage groups were in agreement with previously published maps (Bishop et al., 1994; Barendse et al., 1997) and the linkage map on the web site of the Meat Animal Research Center (<http://www.marc.usda.gov/>).

In the initial analysis, without inclusion of cofactors, we detected 13 QTL that exceeded the 5% chromosome-wise significance level in the across-family analysis. These QTL were located on 8 chromosomes (BTA6, 7, 9, 11, 13, 15, 20, and 29). Two QTL were significant at the genome level. When including possible QTL from the initial analysis as cofactors in the following analyses, both the number of QTL detected and the test statistics increased in most cases. We found 30 QTL at the 5% chromosome-wise significance level when including cofactors, and 15 of these reached genome-wise significance.

All QTL detected with F -values exceeding the 5% chromosome-wise threshold in the across-family analysis without cofactors are given in Table 2. Results from the analysis with cofactors are given in Table 3. The proportion of variance explained by cofactors for the different traits was as follows: NR56_{heifer} 12%, INS_{heifer} 7%, NR56_{cow} 38%, INS_{cow} 24%, FTR 24%, HS 39%, CAL_{dir} 13%, STI_{dir} 8%, CAL_{mat} 37%, and STI_{mat} 31%. In addition to the results that were significant in the across-family analysis, several QTL were found to be segregating only in individual families (data not shown). The within-family analysis provided information about which families segregate for a certain QTL. A very large effect in one family can make a QTL significant even in the across-family analysis. Smaller effects in a similar position by several families can also make a QTL significant.

Nonreturn Rate

Heifers. We detected one QTL for NR56_{heifer} on BTA9 significant at the genome level in the across-family analysis. In the within-family analysis, 5 families segregated ($P_{\text{chromosome}} < 0.10$) for NR56_{heifer} on BTA9. The results did not change after inclusion of cofactors in the analysis.

First-Lactation Cows. Initially we detected QTL for NR56_{cow} on BTA15 and 20. The QTL on BTA20 was significant at the genome level. When cofactors were added, we detected 6 QTL for NR56_{cow}, on BTA1, 11, 15, 18, 20, and 29. Of these, 5 were significant at the genome level (Table 3).

Table 2. Results from the initial analysis without cofactors¹

BTA ²	Trait ³	Marker or marker bracket	<i>P</i>		Family ⁴
			Chromosome	Genome	
6	CAL _{dir}	BM143	**		5,7,10
	CAL _{mat}	BM1329	**		3,5,6
7	STI _{mat}	BM6105	*		1,4,8
9	INS _{heifer}	TGLA73	*		1,8
	NR56 _{heifer}	TGLA73	***	**	1,2,5,8,9
11	INS _{cow}	ILSTS036	*		5
	STI _{mat}	BMS7169	*		3,4,5,9
13	HS	AGLA232	*		5,7
	CAL _{mat}	BMS1352	*		6,9
15	NR56 _{cow}	NCAM	**		3,4,7
	CAL _{mat}	NCAM	*		2,3,9
20	NR56 _{cow}	BMS1282	***	*	1,5,6,10
29	INS _{cow}	BMS1244–BMC8012	*		1,2,6

¹Only results with a significance of $P < 0.05$ are shown.

²BTA = *Bos taurus* autosome.

³CAL_{dir} = Calving performance (direct effect); CAL_{mat} = calving performance (maternal effect); CFI = interval calving to first insemination; FTR = fertility treatments; HS = heat intensity score; INS_{cow} = number of inseminations (first-lactation cows); INS_{heifer} = number of inseminations (heifers); NR56_{cow} = nonreturn rate of 56 d (first-lactation cows); NR56_{heifer} = nonreturn rate of 56 d (heifers); STI_{dir} = stillbirth (direct effect); STI_{mat} = stillbirth (maternal effect).

⁴Code number of segregating ($P < 0.10$) families.

* $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$.

Number of Inseminations

Heifers. A QTL for INS_{heifer} was found on BTA9 when analyzing across families without cofactors. Two families segregated for this QTL, and there was no difference in the result after adding cofactors to the analysis. The highest F-value was observed in the same position as the QTL for NR56_{heifer}.

First-Lactation Cows. In the first analysis, 2 QTL affecting INS_{cow} were significant at the chromosome level; the QTL were located on BTA11 and 29. After including cofactors in the analysis, 2 additional QTL were detected, on BTA3 and 15. The QTL found in the initial analysis received higher test statistics after the use of cofactors. The QTL on BTA11 reached genome-wide significance and the number of segregating families increased from 1 to 5 after adding cofactors to the analysis.

Fertility Treatments

In the initial analysis, no QTL for fertility treatments were detected in the across-family analysis at the chromosome-wise 5% significance level. However, 2 QTL located on BTA1 and 11 reached the level for inclusion as cofactors ($P < 0.10$). When analyzing with cofactors, 3 QTL were detected, on BTA1, 3, and 22. The number of families segregating for these QTL varied from 1 to 3.

Interval from Calving to First Insemination

No QTL were found in the across-family analysis for the trait interval from calving to first insemination,

thus no cofactors could be used in the analysis. Only a few individual families with a significant segregation were observed.

Heat Intensity Score

In the analysis without cofactors, 1 QTL was detected on BTA13. In the subsequent analysis with cofactors, 5 QTL were found on BTA4, 7, 9, 13, and 25. Of these, the QTL on BTA7 and 9 were significant at the genome level; 2 and 3 families segregated for these QTL, respectively.

Stillbirth

Direct. No QTL with chromosome-wise significance of 5% was found for STI_{dir}, but a QTL on BTA14 ($P < 0.10$) was included in the cofactor analysis. The cofactor analysis did not increase the test statistics and no QTL was found in the across-family analysis for this trait. However, 3 individual families were segregating for STI_{dir} in the within-family analysis (e.g., on BTA1, 2, 3, 11).

Maternal. In the first analysis without cofactors, we detected 2 QTL for STI_{mat} on BTA7 and 11. After inclusion of cofactors, 2 additional QTL were detected, on BTA4 and 19, and the previously found QTL reached genome-wise significance.

Calving Performance

Direct. When analyzing across families without cofactors, we detected one QTL for CAL_{dir} on BTA6 at the

Table 3. Results¹ from the cofactor analysis

BTA ²	Trait ³	Marker or marker bracket	<i>P</i>		Family ⁴	Number of cofactors
			Chromosome	Genome		
1	NR56 _{cow}	ILSTS104–BM6506	*		4,9	6
	FTR	TGLA49	**		2,5,7	4
3	INS _{cow}	INRA197	*		2,10	4
	FTR	BM2924	**		7	4
4	HS	MGTG4B	*		4,6	6
	STI _{mat}	BMS1237–HUIJ673	*		1,3,8	4
6	CAL _{dir}	BM143	***	*	5,7,10	1
	CAL _{mat}	BM1329	***	*	2,3,5	5
7	HS	BMS522	***	**	2,6	6
	STI _{mat}	BM6105	***	**	1,4,8	4
9	HS	BMS817	***	*	2,6,9	6
	INS _{heifer}	TGLA73	*		1,8	1
	NR56 _{heifer}	TGLA73	***	**	1,2,5,8,9	1
11	INS _{cow}	ILSTS036	***	*	3,5,6,7,8	4
	NR56 _{cow}	INRA177	***	*	1,2,4,10	6
	STI _{mat}	BMS7169	***	*	3,5,8,9	4
13	HS	AGLA232	**		5,6,7	6
	CAL _{mat}	BMS1352	***	**	2,3,6,9,10	5
15	INS _{cow}	NCAM	*		3,5	4
	NR56 _{cow}	NCAM	***	**	1,3,4,7	6
	CAL _{mat}	BR3510–NCAM	**		2,7,9	5
18	NR56 _{cow}	BMS2639	***	**	2,3,4,7	6
	CAL _{mat}	BMS2785	***	*	3,10	5
19	STI _{mat}	BMC1013	**		5,9	4
20	NR56 _{cow}	BMS1282	***	**	1,4,5,6,7,10	6
22	FTR	BM4102	*		3,7,8	4
25	HS	RM404	**		1,6,7	6
29	INS _{cow}	BMS1244–BMC8012	**		1,2,6	4
	NR56 _{cow}	BMS1600–ILSTS81	***	*	1,2	6
	CAL _{mat}	BMS1600–ILSTS81	*		6,7	5

¹Only results with a significance of $P < 0.05$ are shown.

²BTA = *Bos taurus* autosome.

³CAL_{dir} = Calving performance (direct effect); CAL_{mat} = calving performance (maternal effect); CFI = interval calving to first insemination; FTR = fertility treatments; HS = heat intensity score; INS_{cow} = number of inseminations (first-lactation cows); INS_{heifer} = number of inseminations (heifers); NR56_{cow} = nonreturn rate of 56 d (first-lactation cows); NR56_{heifer} = nonreturn rate of 56 d (heifers); STI_{dir} = stillbirth (direct effect); STI_{mat} = stillbirth (maternal effect).

⁴Code number of segregating ($P < 0.10$) families.

* $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$.

1% chromosome-wise significance level. When including cofactors in the analysis, the QTL on BTA6 became significant at the genome level. No new QTL were detected and the position remained the same on BTA6.

Maternal. Initially 3 QTL (on BTA6, 13, and 15) were detected for CAL_{mat} when analyzing without cofactors. After cofactors were added to the analysis, 2 additional QTL were found, on BTA18 and 29. The test statistics increased with cofactors in the analysis and 3 QTL (on BTA6, 13, and 18) exceeded the genome-wise significance threshold. In the within-family analysis, 5 families segregated for the QTL on BTA13.

DISCUSSION

When the analysis was performed without inclusion of cofactors, we detected 13 suggestive QTL that were located on 8 chromosomes. When cofactors were used,

11 of the suggestive QTL reached a higher significance level, and 2 remained at the same level. The cofactor analysis also detected QTL that did not reach the significance threshold in the initial analysis. Six new QTL reached genome-wise significance in the cofactor analysis; they were located on the same 8 chromosomes as the QTL from the initial analysis and also on BTA18. The positions of the QTL did not change more than a few centimorgans after inclusion of cofactors.

For the traits NR and INS, we considered cow performance and heifer performance as 2 different traits. More QTL were detected for the cow performance traits compared with the heifer traits and the locations of the QTL did not correspond very well between the traits. However, it is likely that partly different genes are responsible for the fertility of a nonproducing virgin heifer compared with the fertility of a high-producing lactating cow. When the dietary intake in early lacta-

tion does not meet the energy requirements of high milk production, the cow enters a stage of negative energy balance. In this situation, body reserves will be reallocated for production, which may lead to a reduction in fertility (Van der Lende, 1997; Wall et al., 2003).

In general, the test statistics for analyzed QTL tended to increase considerably after cofactors were added. By including cofactors in the analysis, the residual variance will decrease because of the variance explained by the cofactors. This results in an increased chance of detecting QTL. The variance explained by cofactors varied between 7 and 39% between the different traits, depending in part on number of cofactors used in the analyses. This variance gives an estimate of the total variance accounted for by all QTL found for a certain trait, provided that these cofactors are true QTL. Sahana et al. (2004) tested the effects of cofactors on power of detection and false discovery rate (type 1 error) in QTL mapping by simulation. They concluded that cofactor analysis increases the number of false-positive QTL and the biggest increase was seen in low power experiments. However, the power to detect QTL increased when a low heritability trait was analyzed and a liberal threshold for cofactors was used.

It is necessary to take into consideration the higher false discovery rate when cofactors are included in the analysis. A more stringent threshold should be applied to determine QTL when cofactors are used. Because of the rather liberal threshold that was used for inclusion of cofactors in these analyses, some of the results are likely to be false positives and require further validation. The QTL detected in this study that did not reach genome-wide significance in the cofactor analysis must be interpreted with caution. We have chosen to mainly discuss the results that reached the genome-wide significance in the cofactor analysis.

Nonreturn Rate

The only trait for which we detected genome-wide significant QTL in the initial analysis was NR. For this trait, we found 2 QTL in the initial analysis and 6 QTL in the cofactor analysis at genome-wide significance. The QTL on BTA9 affecting NR in heifers was supported by the findings of Schrooten et al. (2000); they also detected a QTL for NR in the same position. Five of the 10 families segregated for this QTL and 4 of these families showed highest test statistics in the same region, toward the end of BTA9. The effect of the QTL in the segregating families ranged from 0.5 to 1.1 standard deviations of the DYD.

Kuhn et al. (2003) mapped a QTL for NR on BTA18 to the same half of the chromosome as we mapped a QTL for the same trait, and Ashwell et al. (2004) found

indications of a QTL affecting pregnancy rate close to our QTL on BTA18. No QTL for NR have been identified before on BTA11, 15, 20, or 29. In a study on Finnish Ayrshire cattle, Schulman et al. (2003) found QTL for the trait days open on BTA11, 20, and 29. Days open was defined as the number of days from calving to the next pregnancy.

Number of Inseminations

Only one QTL (on BTA11) for INS reached the genome-wide significance threshold in the cofactor analysis. To our knowledge, no QTL has previously been mapped for this trait. However, INS and NR are highly correlated traits (Wall et al., 2003) and most of the suggestive QTL for INS in the cofactor analysis were found close to our QTL affecting NR, but the test statistics differed between the traits.

Fertility Treatments

No QTL for FTR was significant in the initial analysis or reached the genome-wide level in the cofactor analysis. Quantitative trait loci for FTR have previously only been described by Schulman et al. (2003) who detected several QTL for this trait. The only result that we could support to some degree was on BTA1 where we found a QTL at the 1% chromosome-wide significance level in the cofactor analysis. One reason for the few QTL for this trait may be that the trait is a combination of subtraits with different physiological expressions. Examples of reproductive disturbances in the Swedish recording system are: endometritis, cystic ovaries, other ovarian problems, and other gynecological problems.

Interval Calving to First Insemination

No QTL was significant in the across-family analysis for the trait CFI in this study. Three families segregated in the within-family analysis on BTA4, but in different positions and were thus not sufficient to make the QTL significant in the across family analysis. One reason for not detecting any significant QTL for CFI may be that the trait does not very well reflect the physiology of the cow, as it is largely influenced by the farmer's decision on when to do the first insemination, and also by the skill in heat detection. Roxström et al. (2001) found that herd-year effects accounted for a greater proportion of the total variance for CFI compared with other fertility traits. Only one study has mapped QTL for this trait before (Schrooten et al., 2000), and they found QTL on BTA6 and 17 affecting the interval from calving to first insemination.

Heat Intensity Score

We were able to detect a few QTL with an effect on HS. No QTL have been described previously for this trait. The only fertility trait QTL that have been found close to any of our heat intensity QTL was on BTA7 where Boichard et al. (2003) detected a QTL for postpartum fertility (success or failure of insemination).

Calving Performance and Stillbirth

The limited number of QTL for direct effects on CAL and STI may partly be explained by the fact that only 8 out of the 10 families had phenotypic records on these traits. There were no common QTL found for STI and CAL in the across family analysis. Although traits are highly correlated genetically (0.83 to 0.85; Steinbock et al., accepted), several other factors affect the traits independently. Berglund et al. (2003) found by postmortem examination that 46% of the STI were due to difficult calvings and as much as 32% were born with no indication of difficulties at parturition. Thus, we would expect to find QTL with an effect on both STI and CAL, but also QTL that are specific for one of the calving traits only.

The QTL for CAL_{mat} on BTA18 is supported by the findings of Kuhn et al. (2003) who found indications of QTL for both CAL and STI on BTA18. On BTA6 we detected 2 QTL for CAL (direct and maternal effect), which is in agreement with results from Schrooten et al. (2000) who reported a QTL for CAL in the same region. No previous QTL have been reported for CAL on BTA13. Kuhn et al. (2003) however, found a QTL for STI on this chromosome. On BTA11, where we found QTL for STI, no other study has reported QTL for calving traits. Our QTL on BTA7 for STI_{mat} is located on the same end of the chromosome as QTL for STI_{dir} and CAL_{dir} reported by Kuhn et al. (2003).

Chromosome Regions of Particular Interest

Quantitative trait loci regions with effects on more than one trait were found on some of the chromosomes. Quantitative trait loci for calving and fertility traits were found on BTA11, 13, and 15 in the initial analysis and on BTA4, 7, 11, 13, 15, 18, and 29 in the cofactor analysis. On BTA9 we detected the QTL (for NR56_{heifer}) with highest significance in the initial analysis; in this region, we also found QTL for the correlated trait INS_{heifer} and HS. In the previous study on health traits (Holmberg and Andersson-Eklund, 2004), a QTL for mastitis was mapped to the same region on BTA9 as the QTL for fertility traits. On BTA11 we detected 3 QTL (for NR56_{cow}, INS_{cow}, and STI_{mat}) with genome-wide significance in the cofactor analysis. The QTL for

NR56_{cow} was found in the same region as a QTL for mastitis from the previous study and the QTL affecting STI_{mat} was located in the same region as a QTL for SCC. Thus, it seems likely that several different QTL or a few pleiotropic QTL are located on chromosomes 9 and 11.

CONCLUSIONS

Reproduction traits are complex because they consist of several subtraits, and are largely influenced by the environment. Despite the low heritability of the traits analyzed in this study, our results show that it is worthwhile to perform QTL mapping studies on these traits. We have found that it is possible to identify chromosome regions with an effect on fertility and calving traits in the Swedish dairy cattle population. Many of our QTL confirm the findings of previous studies of the same or related traits. This study provides the first step in identifying the underlying genes causing the effects. Our results provide a basis for further work to narrow down the QTL regions. Refinement of the QTL regions is needed before the results can be used in practical breeding.

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