Twelve-year cohort study on the influence of caprine arthritis-encephalitis virus infection on milk yield and composition

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ABSTRACT

This long-term observational cohort study was carried out to evaluate the effect of caprine arthritis-encephalitis virus (CAEV) infection on the quantitative and qualitative characteristics of milk production in dairy goats. For this purpose, a dairy herd comprising both CAEV-infected and uninfected female goats was observed for 12 consecutive years. Records on daily milk yield, somatic cell count (SCC), and contents of the major milk components (fat, protein and lactose) were collected every month. In total, 3,042 records (1,114 from CAEV-positive and 1,928 from CAEV-negative animals) from 177 female goats were used for statistical analysis. The multi-trait repeatability test-day animal model using the derivative-free multivariate analysis package with the average information-REML method was applied to eliminate the influence of factors other than CAEV infection on milk production in goats. The statistical significance of the differences between estimates for seropositive and seronegative goats was evaluated using Student’s t-test. The effect of age of goats (parity) on their serological status was also estimated with the one-trait repeatability test-day model. The serological status of goats was linked to parity: the higher the parity, the greater the probability of CAEV infection. No significant differences between infected and uninfected goats with respect to daily milk yield and SCC were found. On the other hand, the milk of uninfected goats contained more total protein (3.40% vs. 3.35%), fat (3.69% vs. 3.54%), and lactose (4.30% vs. 4.25%) than the milk of infected goats. Even though these differences were highly significant, they were small when expressed numerically.

Key words: caprine arthritis-encephalitis, goat milk, somatic cell count

INTRODUCTION

Caprine arthritis-encephalitis (CAE) is an important infectious disease of goats described for the first time in the United States in 1974 (Cork et al., 1974). It is caused by the virus CAE virus (CAEV), which belongs, together with maedi-visna virus, to the genus Lentivirus, family Retroviridae. The viruses, considered 2 distinct species for many years, were recently reclassified to one species called small ruminant lentiviruses (SRLV) based on their genetic similarity (Shah et al., 2004). Infection with CAEV is widespread in goat populations around the world and is particularly prevalent in dairy goats (Adams et al., 1984). The virus has been reported in Poland and was detected in the majority of Polish breeding goat herds (Kaba et al., 2010a). The disease is characterized by a life-long infection, with the animals eventually showing chronic progressive arthritis. Other symptoms ascribed to CAEV infection are pneumonia, chronic weight loss, encephalomyelitis, and indurative mastitis (Phelps and Smith, 1993). The exact influence of CAEV infection on the mammary glands of goats is still unclear. It is well known that in the pathogenesis of CAE, monocytes, macrophages, and dendritic cells are responsible for establishing life-long infection (Narayan et al., 1982). Thus, infected monocytes can migrate to many organs (including udder) and differentiate into macrophages (Haase, 1986). Infected macrophages are able to secrete inflammatory cytokines, which attract lymphocytes and can induce chronic immune-mediated inflammation of infected tissues (Zink et al., 1990). Several in vitro studies have showed that mammary gland tissue is prone to CAEV infection (Msellii-Lakhal et al., 2001; Lechat et al., 2005; Le Jan et al., 2005); milk epithelial cells are particularly susceptible. It was concluded that the infection could result in activation of the in vivo inflammatory process by recruitment and activation of effector cells for inflammation and immunity (Msellii-Lakhal et al., 2001). This process was confirmed in CAEV-infected goats. Immune-mediated inflammation seems to be the core of CAE pathogenesis (Jolly et al., 1997; Ponti et
al., 2008; Kaba et al., 2011). The influence of the infection on lymphocyte reactivity was also detected (Kaba et al., 2010b). Moreover, during infection, the local immune response in the udder was very strong (Le Jan et al., 2005; Milhau et al., 2005). These observations imply that CAEV infection should have an important influence on milk production in goats.

Thus far, several studies have dealt with the impact of CAEV infection on milk production (Smith and Cutlip, 1988; Lerondelle et al., 1992; Ryan et al., 1993; Greenwood, 1995; Nord and Adnøy, 1997; Luengo et al., 2004; Turin et al., 2005; Leitner et al., 2010). Because the results of these studies were inconclusive and often contradictory, we have attempted to evaluate the influence of CAEV infection on 5 main parameters of milk production; namely, milk yield, SCC, and contents of fat, protein, and lactose in a long-term cohort study.

MATERIALS AND METHODS

Animals and Sampling

The study was carried out over 12 successive years in a herd of approximately 50 dairy goats. Caprine arthritis-encephalitis was confirmed on this farm by serology and virus isolation (Kaba et al., 2009). The animals were kept in a loose barn and fed according to the INRA system (Jarrige, 2002). The goats belonged to 2 dairy breeds: Polish White Improved and Polish Fawn Improved. They were milked mechanically twice a day. The average milk yield during 280 d of lactation was about 800 kg, with 3.35% fat and 3.20% total protein. Milk samples were taken from each goat once a month during the entire lactation periods for 12 yr. The daily milk yield (kg), SCC, and contents of fat (%), protein (%), lactose (%) were evaluated in each milk sample. The fat, protein, and lactose contents were estimated in milk preserved with Broad Spectrum Microtabs II (Bentley, Warsaw, Poland), using a MilkoScan 104A/B (Foss A/S, Hillerød, Denmark). Somatic cells were counted by using a Fossomatic 90 apparatus (Foss A/S).

Serological Testing

All goats were tested serologically for the first time at 4 to 6 mo of age and then each year in November or December during a dry-off period. An immunoenzymatic test (Idexx CAEV/MVV Total Ab Screening Test, Idexx Europe, Hoofdropp, the Netherlands) was used. The test was performed according to the manufacturer’s manual using an ELISA reading device (ICN Flow Tittertek Multiscan Plus Mk11, Labsystems, Espoo, Finland). Goats were ranked as positive or negative. When a goat reacted inconclusively, both lactations—that preceding and that following the inconclusive result—were omitted. If a goat seroconverted, the lactation between the negative and positive result was omitted as well.

Statistical Analysis

In total, 3,042 records (1,114 CAE positive and 1,928 CAE negative) from 177 female goats were used for statistical analysis. The SCC values were transformed to the natural logarithm scale (ln SCC). The analysis was conducted with the multi-trait repeatability test-day animal model using the DMU package with the average information REML (AIREML) method (Madsen and Jansen, 2000). The pedigree information dated back to the fourth generation. Three classes of parity were distinguished, with the third covering all lactations above second. The model used was as follows:

\[ y_{ijklmn} = a_i + p_i + y_{sj} + t_{dk} + SS_l + LSm + P_n + \beta(x_{ijklmn} - x) + (\Sigma bpLPdp)_{ijklmn} + e_{ijklmn}, \]

where \( y_{ijklmn} \) = milk yield, fat, protein, and lactose contents, and SCC, \( a_i \) = animal additive genetic random effect, \( p_i \) = permanent environment of animal random effect, \( y_{sj} \) = year-season of kidding random effect, \( t_{dk} \) = date of the test random effect, \( SS_l \) = serological status of animal fixed effect (\( l = 1,2 \)), \( LSm \) = litter size fixed effect (\( m = 1 \) to 3), \( P_n \) = parity fixed effect (\( n = 1 \) to 3), \( \beta(x_{ijklmn} - x) \) = fixed regression on milk yield for fat, protein, and lactose contents and SCC, \( (\Sigma bpLPdp)_{ijklmn} \) = fixed effect of regression of Legendre polynomials of standardized days in milk (\( p = 1 \) to 4), and \( e_{ijklmn} \) = error.

Legendre polynomials of standardized DIM (Brotherstone et al., 2000) were fitted as fixed covariates within each parity subclass to represent changes in considered traits due to the stage of lactation. Days of lactation were matched as Legendre polynomials from first to fourth degree. Standardized number of days in lactation was the basis of the polynomials.

Days in lactation were standardized according to the following formula:

\[ x_{std} = \frac{2(x - x_{min})}{(x_{max} - x_{min})} - 1, \]

where \( x_{std} \) = standardized number of days in lactation, \( x \) = actual days in lactation, \( x_{max} \) = maximal value of the variable (400 d), and \( x_{min} \) = minimal value of the variable (0) (Sloniewski, 2003).

The fixed regression on milk yield was used for all traits, except for the model for milk yield. The differences between estimates for seropositive and seronegative goats were evaluated using Student’s \( t \)-test.
The effect of age of a goat (parity) on its serological status was also estimated with the one-trait repeatability test-day model using the DMU program (Madsen and Jansen, 2000). The model included parity as fixed effect and the additive genetic effect and permanent environmental effect of individual goat, the date of the test, and year-season of kidding as random effects. The fixed regression on milk yield was used. The differences between parities for serological status of goats were checked using Duncan’s test with Bonferroni adjustment.

The following model was used:

\[ y_{ijklm} = a_i + p_i + y_{sj} + t_{dk} + P_1 + \beta(x_{ijklm} - x) + e_{ijklm}, \]

where \( y_{ijklm} \) = serological status of goats, \( a_i \) = animal additive genetic random effect, \( p_i \) = permanent environment of animal random effect, \( y_{sj} \) = year-season of kidding random effect, \( t_{dk} \) = date of the test random effect, \( P_1 \) = fixed effect of parity (n = 1 to 3), \( \beta(x_{ijklm} - x) \) = fixed regression on milk yield, and \( e_{ijklm} \) = error.

For all statistical calculations, a level of significance of 0.01 was used (\( \alpha \leq 0.01 \)).

**RESULTS**

Seronegative and seropositive goats did not differ with respect to daily milk yield or SCC. However, highly significant differences were found for the main components of milk; milk of healthy goats contained more total protein (3.40% vs. 3.35%, \( P \leq 0.01 \)), fat (3.69% vs. 3.54%, \( P \leq 0.01 \)), and lactose (4.30% vs. 4.25%, \( P \leq 0.01 \)) than the milk of infected goats (Table 1). Moreover, the serological status of a goat was linked to its parity: the higher the parity, the greater the probability of CAEV infection; the probability of infection in 1-yr-old goats was lower by 84% and in 2-yr-old goats by 42% compared with goats aged 3 or more years (\( P \leq 0.01 \); Table 2).

**DISCUSSION**

Caprine arthritis-encephalitis is a chronic progressive disease, so evaluation of its effect on the performance of goats requires a long time. To our knowledge, this observational study evaluating the influence of CAE on milk production has evaluated goats for a period substantially longer than that of other studies. For comparison, the longest previous study (and the most recent) lasted 3 yr (Leitner et al., 2010). A 12-yr period of observation and more than 3,000 records provided reliable data sufficient to draw unambiguous conclusions on the influence of CAEV infection on the quantity and quality of produced milk. The study was conducted in one herd, thus the environmental effect was the same for all animals. By using a pedigree set that takes into account all relations between animals, the accuracy of estimates should be very high (Norman et al., 1991). Moreover, the statistical model applied in the study attempted to eliminate the influence of all important factors other than CAEV infection on milk production of goats. Furthermore, the use of the test-day model, which pertains to the random effect of date of milking, helped to improve the accuracy of estimates (Bishop et al., 1995).

We assumed 2 possible serological statuses of goats in the study: positive (i.e., infected with CAEV) and negative, either uninfected or before seroconversion (infected

<table>
<thead>
<tr>
<th>Item</th>
<th>Parity 1</th>
<th>Parity 2</th>
<th>Parity ≥3</th>
</tr>
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<tbody>
<tr>
<td>Serological status</td>
<td>-0.84(^a)</td>
<td>-0.42(^b)</td>
<td>0.00(^c)</td>
</tr>
</tbody>
</table>

\(^abc\)Solutions within a row with different superscripts differ (\( P \leq 0.01 \)).
within the past several months; Juste et al., 1998). Unlike Nord and Adnøy (1997), we excluded all goats with inconclusive results from the study. Given that a goat can be either infected or uninfected with CAEV, we considered animals with indeterminate results as undiagnosed due to shortcomings of the ELISA test rather than belonging to a third health category. Moreover, we disqualified the lactation between the negative and positive result of the ELISA test because the serological status of a goat in that lactation was indeed unknown. We found this approach more reasonable than creating the third group comprising animals that seroconverted between 2 tests, as done by Leitner et al. (2010). In fact, the group created by Leitner et al. (2010) included infected and naive goats commingled randomly. On the other hand, infected goats periodically become seronegative (Hanson et al., 1996); therefore, a goat that had been diagnosed as seropositive at least twice was deemed infected until the end of its life. In the case of an inconclusive result in a previously seronegative goat, we omitted 2 lactations (preceding and following) because the true health status of the individual was not certain. This was done to maximize the credibility of our results.

Our study confirmed no influence of CAEV infection on the milk yield. One previous study reported a decrease in milk production but only if the allowance of supplementary feed was greatly reduced (Greenwood, 1995). Leitner et al. (2010) noted decreased milk yield but only in primiparous does; the effect disappeared in multiparous does. However, Greenwood (1995) observed reduction of milk production only in multiparous females. In the study of Turin et al. (2005), milk production did not differ between seropositive and sero-negative primiparous goats.

Our study is the first to reveal a highly significant influence (α ≤ 0.01) of CAEV infection on the amount of all 3 main components of milk. Nord and Adnøy (1997) did not observe such changes in 1- or 2-yr-old goats. Turin et al. (2005) noted a reduction in protein concentration, unchanged lactose concentration, and elevated fat concentration in seropositive goats. However, that study was based on a very small number of primiparous goats (13 seropositive and 18 sero-negative), raising concerns about its credibility. Reduction of fat content in milk was noted by Smith and Cutlip (1988). Results similar to ours regarding fat and protein concentrations were obtained by Greenwood (1995) and Leitner et al. (2010) but only in multiparous does if the allowance of supplementary feed was highly reduced. The differences in results might arise because of the age of observed goats. As all the above-mentioned observations were made only on 1- and 2-yr-old goats, reduction in the quality of milk might develop gradually in consecutive lactations. Although our study revealed that CAEV infection reduced fat, protein, and lactose contents in goat milk, the differences were small (Table 1), which likely explains why other studies based on considerably smaller data sets were not able to detect and statistically confirm this relationship.

Several previous studies showed a strong influence of CAEV infection on SCC (Lerondelle et al., 1992; Ryan et al., 1993; Nord and Adnøy, 1997; Sánchez et al., 2001; Turin et al., 2005). However, Nord and Adnøy (1997) observed the increase of SCC only in 2-yr-old does, not in primiparous does, whereas Turin et al. (2005) noted elevation of SCC in primiparous females. The most recent study (Leitner et al., 2010) yielded results consistent with ours: no relationship between the infection and SCC was found. It has been postulated that SCC cannot be the only indicator of the udder infection in goats (Bagnicka et al., 2011). Infections were found to account for less than 10% of the variation in milk SCC, whereas increasing DIM, month of the year, and parity were most important (Wilson et al., 1995). The statistical model used in our study eliminated the influence of factors other than CAEV infection and thus explains our results. On the other hand, Poutrel et al. (1997) found subclinical bacterial infections to be an important factor resulting in elevated SCC in goats. It has also been shown that the udder is a target organ for CAEV infection and infected animals may have subclinical chronic viral mastitis (Kennedy-Stoskopf et al., 1985; Bergonier et al., 2003). Our results do not contradict this observation, as important differences may exist in the reaction of the udder to bacterial and viral infections. Infection with CAEV results in accumulation of macrophages rather than neutrophils (Lerondelle et al., 1992), which are the main leukocytes attracted by a bacterial infection (Paape and Capuco, 1997). Neutrophils are also the main cells contributing to high SCC (Droke et al., 1993). Even if a chronic viral mastitis was present in some CAEV-infected goats in a herd, it did not have to result in an increase in SCC. Moreover, the lack of a significant elevation of SCC suggested no influence of CAE on the prevalence of bacterial mastitis, as was stated by Nord (1997) and Luengo et al. (2004), which seems to contradict the results obtained by Ryan et al. (1993).

Our observation that parity is linked to the probability of CAEV infection (Table 2) confirmed that long-term contact between goats is a route of disease transmission (Peterhans et al., 2004).

CONCLUSIONS

Infection with CAEV did not reduce milk yield or elevate SCC. However, the quality of milk was nega-
tively affected by CAEV infection with respect to total protein, fat, and lactose, albeit to a very limited extent. Whether such an effect on milk quality is sufficient to result in a lesser quality of dairy products is yet to be evaluated.

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