Selection against metabolic diseases

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Abstract

Metabolic stability or resistance to metabolic diseases can be improved by genetic selection. Strategies include direct selection based on clinically observed traits, and indirect selection using indicators or predictors of metabolic diseases. The most prevalent metabolic diseases in dairy cattle, for which genetic parameters were published included: ketosis, displaced abomasum, milk fever, and tetany. In this review we present genetic parameters for these metabolic diseases, discuss possible indicator traits, and give a status of genetic evaluation of metabolic diseases.

Keywords: metabolic disease, genetic parameters

Introduction

Disturbances or dysfunction of metabolic processes can cause metabolic diseases. The health key included in the ICAR guidelines for recording, evaluation and genetic improvement of health traits in dairy cattle (ICAR, 2016) includes a total of 72 metabolic conditions. The incidences of most of them are low, however, others (e.g., ketosis, milk fever) are among the most frequent diseases affecting dairy cattle. Incidences of clinical cases of metabolic diseases vary between studies but were mostly reported to be below 10% of cows per year or parity/lactation (Pryce *et al.*, 2016). Considerably higher incidence rates were found for subclinical metabolic diseases. For example, Ingvartsen (2006) reported an incidence of subclinical ketosis of 34%. Even if subclinical cases per definition do not show signs of disease, subclinical metabolic conditions are

often precursors for other diseases and reasons for reduced production and economic losses. Therefore, prophylactic measures against clinical and subclinical cases should be taken, including optimization of feeding and management and using additive genetic variation in metabolic function, which allows improving metabolic stability or resistance to metabolic diseases in dairy cattle by genetic selection. This can be direct selection based on clinically observed traits, or indirect selection using predictors of metabolic diseases. In this review we present genetic parameters, discuss possible indicator traits, and give a status of genetic evaluation of metabolic diseases.

Traits

This review focuses on the most prevalent metabolic diseases in dairy cattle for which genetic parameters were published: ketosis, displaced abomasum, milk fever, and tetany. Ketosis is associated with negative energy balance and mobilization of body fat, so risk of ketosis is particularly high in early lactation in high yielding cows. The condition is characterized by accumulation of ketone bodies in blood, milk and other body fluids. Reduced appetite leads to a vicious cycle of worsening negative energy balance and ketosis. Displaced abomasum is usually associated with stretching of the abomasal attachments during gestation and increased space in the abdominal cavity after calving. Due to reduced motility of the abomasum, it fills with gas and then displaces, more often to the left than to the right upper abdomen. When displacement is accompanied by torsion, gas accumulation increases and drives displacement further. Milk fever or hypocalcemia is characterized by very low blood calcium. Clinical cases have lower-than-normal body temperature and cows exhibit partial or complete paralysis, typically occurring close to calving. Subclinical milk fever is diagnosed by decreased serum calcium. Tetany or hypomagnesemia occurs if the amount of magnesium is insufficient for maintenance of regular muscle function. Clinical signs include changes in behavior, muscle spasms, convulsions, and paralysis. Tetany can lead to sudden death.

Heritability

Heritability estimates of clinical metabolic diseases were in line with heritability of other health traits. In a review, Pryce *et al.*, (2016) reported that threshold model estimates of heritability were 0.02 to 0.16 for ketosis, 0.12 to 0.35 for displaced abomasum, 0.07 to 0.18 for milk fever and 0.02 for tetany. Linear model estimates were, as expected, in general lower: 0.01 to 0.39 for ketosis, 0.00 to 0.08 for displaced abomasum, 0.01 to 0.08 for milk fever and 0.004 for tetany.

Genetic correlations

Genetic correlations among metabolic diseases were positive, indicating that selection to improve one metabolic disease will result in positive indirect selection responses in others. The genetic correlation estimates were slightly higher, from 0.45 to 0.79, between ketosis and displaced abomasum (Zwald *et al.*, 2004; Parker Gaddis *et al.*, 2014; Jamrozik *et al.*, 2016a) than between ketosis and milk fever, which ranged from 0.19 to 0.45 (Heringstad *et al.*, 2005; Ederer, 2014). Metabolic diseases have also been found to be positively genetically correlated to other disease traits, such as mastitis and metritis (e.g. Koeck *et al.*, 2012). This implies that selection for general disease resistance and robustness may be possible. There was a lack of consistency in genetic correlation estimates between metabolic diseases and milk production traits. Limited

numbers of studies, small datasets, large standard errors, and large ranges of estimates make it difficult to draw conclusions. Better estimates of the genetic correlations to milk production traits are needed to understand the consequences of selection.

Correlated selection responses for ketosis were reported from a selection experiment with Norwegian Red, where selection for increased milk production resulted in unfavorable indirect selection response for disease incidences (clinical mastitis and ketosis), while direct selection for low clinical mastitis resulted in a favorable genetic trend for ketosis as a correlated selection response (Heringstad *et al.*, 2007).

Genetic evaluation

A few countries have implemented routine genetic and genomic evaluation of metabolic disorders based on direct health traits so far. In Norway, ketosis and milk fever have been part of the sub-index "other diseases", which since 1978 has been included in the total merit index of Norwegian Red (Heringstad and Østerås, 2013). Favorable genetic trends for ketosis in the Norwegian Red population (Heringstad *et al.*, 2007) illustrates that genetic improvement for metabolic diseases is possible. Also Denmark, Finland and Sweden include breeding values for metabolic diseases in "other diseases", a sub-index of the Nordic Total Merit (NAV, 2016). Since 2010, Austria (and Germany) have routine genetic evaluation of milk fever and preliminary evaluation for other metabolic diseases in Fleckvieh (Fuerst *et al.*, 2010), and Brown Swiss since 2013. For German Holsteins, the prototype of genetic evaluations for health traits includes ketosis, milk fever and left-displaced abomasum. In Canada, genetic evaluations for metabolic diseases (clinical and subclinical ketosis and displaced abomasum) for Holsteins, Ayrshires and Jerseys will be implemented in December 2016 (Jamrozik *et al.*, 2016b). Based on the current research activity it is likely that conventional and also genomic breeding values for metabolic diseases will become available in many other countries and populations within the next decade.

Direct selection requires large-scale recording of disease traits. Alternatively, indicators of metabolic diseases can provide information to be used in genetic evaluation.

Possible indicator traits

Challenges related to disease recording and under-reporting, and difficulties in diagnosis of subclinical cases of metabolic disorders have resulted in an increasing interest in predictors. These can be sensor data or results of milk or blood tests, such as ß-Hydroxybutyrate (BHB), changes in body condition score (BCS), changes in body weight or predictors based on data from routine milk recording (e.g., milk mid-infrared spectral data, MIR). Predictors can be used for genetic evaluation, as well as for diagnosis of subclinical cases, risk assessment and herd management.

Increased automation and use of advanced sensors provide new opportunities and solutions. Advanced management systems combining data from multiple sources to predict risk and detect possible health problems, such as metabolic diseases, are developing. However, reliabilities are often not yet convincing, implying the need for further research.

Many of the metabolic diseases are associated with negative energy balance in early lactation. BCS is a subjective measure of an animal's body reserves, and BCS changes can be used to quantify mobilization of body reserves. Automated weighing and automated scoring of BCS (camera) are examples of new technology that can provide frequent and objective measures of new phenotypes and enable new strategies for

assessment of e.g. energy balance. Moderate genetic correlations have been estimated between digestive / metabolic diseases and both BCS (Dechow et al., 2004; Jamrozik *et al.*, 2016a) and body weight change (Frigo *et al.*, 2010).

MIR analyses of milk samples can be used for evaluation of subclinical disease. This has the potential to substantially increase the available phenotype information for subclinical disease, as MIR is established and used in standard analysis for milk recording. MIR has been found useful for screening purposes (healthy cows vs. cows at risk), but so far prediction accuracy is insufficient for ketosis parameters (e.g., de Roos *et al.*, 2007; Grelet *et al.*, 2016b). MIR can also be used to predict energy balance (McParland *et al.*, 2014).

Concentration of BHB in blood is the gold standard diagnosis of ketosis. However, because blood sampling is expensive and not practical for routine recording purposes, alternative predictors have been explored, including fat-to-protein ratio and milk fatty acid profiles. The potential of using MIR for prediction of BHB and acetone in milk have also been investigated in several studies (Gengler *et al.*, 2016; Grelet *et al.*, 2016a,b).

Conclusions

Direct selection to reduce metabolic diseases is possible. However, lack of recording of direct disease traits is a challenge. Several potential indicator traits have been suggested for predicting metabolic diseases, and more applications for indirect traits for metabolic stability are expected with the continuous increase of automated data recording. New phenotypes, including better tools for diagnosis of subclinical cases, may support more efficient selection against metabolic diseases.

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