SELECTION AGAINST METABOLIC DISEASES

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Abstract: Metabolic diseases, such as ketosis and milk fever, are among the most common diseases affecting dairy cattle. Genetic improvement of ability to resist metabolic diseases can be achieved by direct selection with genetic evaluation based on clinically observed traits, or by indirect selection based on indicators or predictors of metabolic diseases. The most prevalent metabolic diseases in dairy cattle, for which genetic parameters have been published, are ketosis, displaced abomasum, milk fever, and tetany. In this review we present genetic parameters for these metabolic diseases, give a status of genetic and genomic evaluations, and discuss possible indicator traits

Keywords: heritability, metabolic disease, genetic correlation, genetic evaluation, indicator traits

Introduction

Disturbances or dysfunction of one or more of the metabolic processes can cause diseases. For dairy cattle a total of 72 metabolic conditions were described in the health key of the "ICAR guidelines for recording, evaluation and genetic improvement of health traits in dairy cattle" (ICAR, 2017). Most of these are rare, but some, such as ketosis and milk fever, are among the most frequent diseases affecting dairy cattle. The reported incidences of clinical metabolic diseases were, in most cases, below 10% of cows per year or parity/lactation (Pryce et al., 2016). Incidence rates of subclinical metabolic diseases were considerably higher (e.g., Ingvartsen, 2006). One strategy to reduce the occurrence of metabolic disease is genetic selection. Metabolic stability or resistance to metabolic diseases in dairy cattle can be improved genetically by direct selection based on clinically observed traits, or by indirect selection using predictors of metabolic diseases. This review focuses on the most prevalent metabolic diseases in dairy cattle for which genetic

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parameters have been published: ketosis, displaced abomasum, milk fever, and tetany. We present genetic parameter estimates for these diseases, provide the status by country of genetic evaluations of metabolic diseases and discuss possible indicator traits that can be used to increase the accuracy of selection.

Traits

Ketosis is associated with negative energy balance and mobilization of body fat. The risk of ketosis is, therefore, greatest for high-yielding cows in early lactation. Ketosis is characterized by the 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 and, if accompanied by torsion, gas accumulation increases and drives displacement further. Milk fever, or hypocalcemia, typically occurs close to calving and is characterized by very low blood calcium. Clinically diagnosed cows have a lower-than-normal body temperature and exhibit partial or complete paralysis. 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 metabolic diseases were in general low (Table 1), and in line with heritabilities of other health traits. In a recent review, Pryce et al. (2016) reported heritability estimates of clinical metabolic diseases that ranged from 0.02 to 0.35 from threshold models, and from 0.00 to 0.39 for linear models. Linear model estimates were, as expected, generally lower than threshold model estimates (Table 1).

Table 1. Range of heritability estimates of clinical metabolic disease (from Pryce et al., 2016)

Trait	Threshold model	Linear model
Ketosis	0.02 – 0.16	0.01 – 0.39
Displaced abomasum	0.12 – 0.35	0.00 – 0.08
Milk fever	0.07 – 0.18	0.01 – 0.08
Tetany	0.02	0.004

The heritability estimates summarized in Table 1 were from different breeds (Holstein, Norwegian Red, Austrian Fleckvieh), some of the studies were based on veterinary treatment data while others used farmer-recorded data, and the number of cows varied from around 2,000 to 370,000.

Genetic Correlations

There were a few published estimates of genetic correlations among metabolic diseases. Estimated genetic correlation between ketosis and displaced abomasum were positive and stronger, ranging from 0.45 to 0.79 (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). Positive genetic correlations indicate that selection to improve one metabolic disease will result in positive indirect selection responses in others. Metabolic diseases were also found to be positively genetically correlated to other disease traits, such as mastitis and metritis (Table 2). This implies that selection for general disease resistance and robustness may be possible. Genetic correlations between metabolic diseases and other disease traits varied from -0.21 to 0.64 (Table 2). Although most correlations were positive, a wide range of estimates were found for most trait combinations, and the results should, therefore, be interpreted with caution.

Table 2. Genetic correlations between metabolic diseases and other diseases (from Pryce et al., 2016) – range of estimates

	Ketosis	Displaced abomasum	Milk fever
Retained placenta	-0.21 – 0.26	-0.07 – 0.42	-0.04 – 0.18
Cystic ovaries	-0.19 – 0.42	-0.11 – 0.26	
Lameness	-0.10 – 0.25	-0.13 – 0.31	
Mastitis	-0.20 – 0.36	0.02 – 0.20	0.12 – 0.64
Metritis	0.17 – 0,32	0.08 – 0.44	0.08

There was also a lack of consistency in estimates of genetic correlation between metabolic diseases and milk production traits (Pryce et al., 2016). Limited numbers of studies, small datasets, large standard errors, and large ranges of estimates make it difficult to draw conclusions. Better estimates of genetic correlations with milk production traits, using data from large studies, are needed to understand the consequences of selection.

Correlated Selection Responses

Correlated selection responses for ketosis were reported from a selection experiment with Norwegian Red cows, where selection for increased milk production resulted in unfavorable indirect selection responses 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). Favorable genetic trends for ketosis in the Norwegian Red population (Heringstad et al., 2007) illustrates that genetic improvement for metabolic diseases is possible.

Genetic Evaluation

Routine genetic and genomic evaluation of metabolic disorders based on direct health traits have been implemented in some countries. In Norway, ketosis and milk fever have been included in the total merit index of the Norwegian Red breed since the 1970's, as part of the trait group "other diseases" (Heringstad and Østerås, 2013). In their joint evaluation, Denmark, Finland, and Sweden include breeding values for metabolic diseases in "general health", a sub-index of the Nordic Total Merit (NAV, 2017). Austria (and Germany) have had routine genetic evaluation of milk fever and preliminary evaluation for other metabolic diseases in Fleckvieh since 2010 (Fuerst et al., 2011), and Brown Swiss since 2013. For German Holsteins, the prototype of genetic evaluations for health traits includes ketosis, milk fever and left-displaced abomasum. Canada started genetic evaluations for metabolic diseases (clinical and subclinical ketosis and displaced abomasum) for Holsteins, Ayrshires, and Jerseys in 2016 (Jamrozik et al., 2016b). Zoetis Genetics (Kalamazoo, MI, USA) began publishing breeding values for six health traits, including displaced abomasum and ketosis, in 2016 for U.S. Holsteins as part of a commercial genotyping product (Vukasinovic et al., 2016). Other countries publish breeding values for ketosis based on indicator traits, e.g. the genetic evaluation for ketosis in the Netherlands is based on Fourier transform infrared spectroscopy (FTIR) measurements of milk acetone and milk ß-hydroxybutyrate acid (BHB) (Vosman et al., 2015). Based on current research activities, it is likely that breeding values for metabolic diseases will become available in many more countries and populations in the (near) future.

Possible Indicator Traits

Direct selection requires large-scale recording of disease traits. Challenges related to lack of recording of direct health traits, as well as difficulties in diagnosis of subclinical cases of metabolic disorders have resulted in an increasing interest for predictors. Predictors can be used for diagnosis of subclinical cases, risk assessment and herd management, but also for genetic evaluation. There are several possible indicator traits that can be used to predict metabolic diseases. 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.

Concentration of BHB in blood is the gold standard diagnosis of ketosis. However, blood sampling is expensive and not practical for routine recording purposes, so alternative predictors have been explored, including fat-to-protein ratio and milk fatty acid profiles. Fuerst-Waltl and Egger-Danner (2017) evaluated the use of the BHB milk test. The heritability was 0.05 in Fleckvieh (Simmental) with a genetic correlation of 0.89 to clinical ketosis. The potential of using mid-infrared (MIR) spectral data for prediction of BHB and acetone in milk have also been investigated in several studies (Gengler et al., 2016; Grelet et al., 2016a, b).

MIR analyses of milk samples can be used to evaluate 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 prediction accuracy has so far been 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).

Many of the metabolic diseases are associated with negative energy balance in early lactation. Body condition score (BCS) is a subjective measure of an animal's body reserves, and changes in BCS 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; Zottl et al. 2016; Fuerst-Waltl and Egger-Danner, 2017) and body weight change (Frigo et al., 2010).

Conclusions

Direct selection to reduce metabolic diseases is possible. However, the lack of recording of direct health traits is a challenge. Several potential indicator traits have been suggested for predicting metabolic diseases. More uses of indirect traits for predicting metabolic stability are expected with the increase in 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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