Hyperketolactia occuring before or after artificial insemination and monitored in milk samples is associated with a decrease in conception in lactating dairy cows

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Abstract

The reproductive performance of dairy cows is a key parameter of profitability and sustainability, affected by many factors, such as a Negative Energy Balance (NEB). NEB leads to ketosis, characterized by an excessive production of circulating ketone bodies, like acetone and beta-hydroxybutyrate (BHBA) after calving. Estimation of milk Acetone and BHBA concentrations are now routinely available through new algorithms developed on the mid infrared spectroscopy profiles (MIR spectrum), providing large datasets. This offers new opportunities to study the changes in conception rates, in relation to hyperketolactia (HKL) around artificial insemination (AI). In this study, data were collected from a Milk Recording Program in West part of France during years 2013 to 2016.

Lactation characteristics and test-day milk results for all lactations has been included, as well as milk concentrations of acetone and BHBA, and data on artificial insemination. For each AI, conception was considered as a binary trait and defined as successful if it was followed by a calving after a referent pregnancy period. Many thresholds were considered and tested as positive test to define cows with HKL, which were then categorized into four classes according to the HKL dynamics before and after AI.

A two-step statistical analysis was performed, using R software. First, the best thresholds to define the categorical variables SCC, DIM (Day In Milk) and 305d MY (Milking Year) to be included in the final logistic regression (second step) were obtained through generalized additive models. Then, a logistic regression with a Poisson correction was performed, using a step-by-step procedure to include explanatory variables. The final model included the HKL categorical variables defined by the different Acetone and BHBA thresholds and was adjusted by the variables DIM, parity, and 305d MY, and herd as a random variable. SSC dynamics, DIM, 305d MY and parity were significantly associated with conception success in all models. No interaction between the above mentioned variables or with HKL was detected.

HKL defined by Acetone or BHBA concentrations before or after AI was significantly associated with a decrease in conception, depending on the threshold, the milk component and the class (HL, HH, LH). High milk BHBA values were associated with a 4 to 14% less likely conception compared to low ones, whatever the BHBA increase is seen before AI, after AI or both. High Acetone after AI was associated with a more

than 10% less likely conception for all thresholds > 0.10 mM, but not before AI. The significant association between HKL after AI and conception has never been reported before.

The negative association between HKL and reproductive performance is consensual and based on pathophysiological and epidemiological evidence. However, the potential physiological mechanisms to explain such association remain not completely defined. The present results suggest that ketosis should be considered as a risk factor for deteriorated reproduction performances and consequently should be of interest for farm advisors.

Key words: hyperketolactia, conception, BHBA, acetone, dairy cows.

Introduction

The reproductive performance of dairy cows is a key parameter of profitability and sustainability. Many factors affect reproductive performance, such as a Negative Energy Balance (NEB). NEB leads to fat mobilization characterized by an excessive production of circulating ketone bodies, like acetone and beta- hydroxybutyrate (BHBA) after calving (Duffield *et al.*, 1998), which defines Ketosis. Two recent meta- analysis highlighted that a decrease in reproduction performance were associated with hyperketonemia (Raboisson *et al.*, 2014, Abdelli *et al.*, 2017).

Estimation of milk Acetone and BHBA concentrations are now routinely available through new algorithms developed on the mid infrared spectroscopy profiles (MIR spectrum). Large datasets available on milk ketones offer new opportunities to study outcomes associated with subclinical ketosis or hyperketonemia. The aim of this presentation is to quantify the changes in conception rates, in relation to hyperketolactia (HKL) around artificial insemination (AI).

Materials and methods

Data and variables

Data were collected from a Milk Recording Program in West part of France (BCEL Ouest; *http://www.bcel- ouest.fr*) during years 2013 to 2016. Lactation characteristics and test-day milk results for all lactations has been included. Data on artificial insemination were available and collected using MySQL software (MySQL, version 5.0, Oracle Corp., Redwood City, CA). For each AI, conception was considered as a binary trait and defined as successful if it was followed by a calving after a referent pregnancy period.

Milk concentrations of acetone and BHBA were measured during 4 months after calving in the local official laboratory for milk analysis (Mylab *http://www.labo-mylab.fr/,* with a MilkoScan®-FOSS analyzer, using the Fourier transform mid-infrared (FT-MIR) spectrometry, after a specific calibration to predict acetone and BHBA contents. Many thresholds were considered and tested as positive test to define cows with HKL, which were then categorized into four classes according to the HKL dynamics for each AI and each threshold of Acetone or BHBA.

Table 1. Classes defining the HKL dynamic before and after AI.

	Dynamic after AI (acetone or BHBA)	
Dynamic before AI (acetone or BHBA)	**Low**	**High**
Low	LL	LH
High	HL	HH

Statistical analysis

Data were analyzed using R (version 2.10.1, 2009–12–14, The R Foundation for Statistical Computing, Vienna, Austria). A two-step statistical analysis was performed. First, the best thresholds to define the categorical variables SCC, DIM (Day In Milk) and 305d MY (Milking Year) to be included in the final logistic regression (second step) were obtained through generalized additive models (GAM, package gam). Then, a logistic regression with a Poisson correction was performed using the package nlme, using a step- by-step procedure to include explanatory variables. The final model included the HKL categorical variables defined by the different Acetone and BHBA thresholds and was adjusted by the categorical variables DIM and parity, and the continuous variable 305d MY. All models included herd as a random variable and were applied either to the first AI following each calving or to all AIs.

Results

SSC dynamics, DIM, 305d MY and parity were significantly associated with conception success in all models. No interaction between the above mentioned variables or with HKL was detected. HKL defined by Acetone or BHBA concentrations before or after AI was significantly associated with a decrease in conception, depending on the threshold, the milk component and the class (HL, HH, LH). High milk BHBA values were associated with a 4 to 14% less likely conception compared to low ones, whatever the BHBA increase is seen before AI, after AI or both. High Acetone after AI was associated with a more than 10% less likely conception for all thresholds > 0.10 mM. Acetone before AI and conception were not associated.

Discussion

The negative association between HKL and reproductive performance is consensual and based on pathophysiological and epidemiological evidence (Raboisson *et al.*, 2014, Abdelli *et al.*, 2017). These associations are lower than the ones reported in previous trials. However, previously published models did not always include

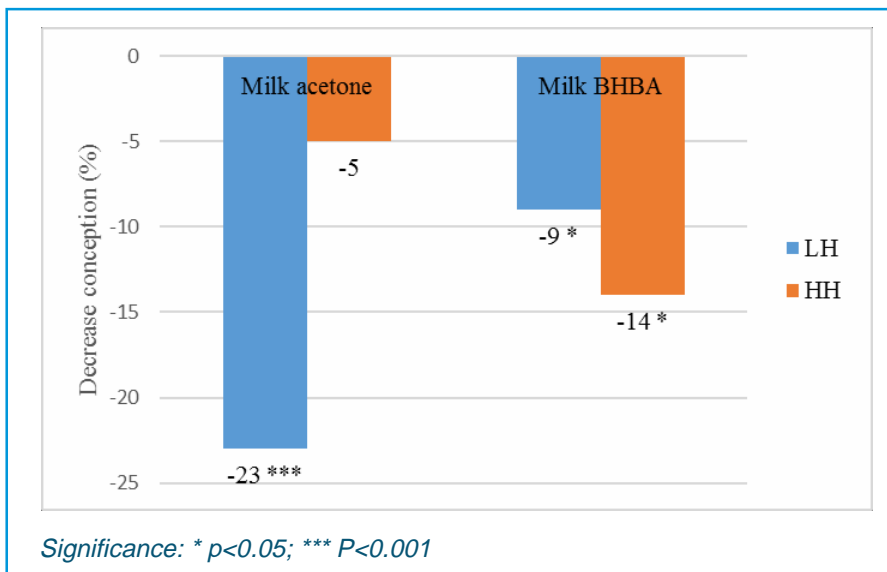*Significance: * p<0.05; *** P<0.001*

Figure 1. Percent decrease conception in case of HKL, compared to the LL class (threshold=0.2 mM).

co-variables, which strongly influences the coefficient value of the subclinical ketosis variable (Raboisson *et al.*, 2014). The lack of association between high Acetone before AI and conception remain unexplained.

The significant association between HKL after AI and conception has never been reported before. However, the potential physiological mechanisms to explain such association remain not completely defined.

Conclusion

The present work confirmed the link between high ketones in dairy cows and conception success, and highlight the association between HKL after AI and conception rate, what has never been demonstrated up to now. High ketones in advanced lactation are likely to be consecutive from various

primary disorders (secondary ketosis). Even if these situations are not primary ketosis, the present results suggest that it should be considered as a risk factor for deteriorated reproduction performances and consequently should be of interest for farm advisors.

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