J. Dairy Sci. 100:1–18
https://doi.org/10.3168/jds.2017-12908

Urinary purine derivatives as a tool to estimate dry matter intake in cattle: A meta-analysis

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ABSTRACT

The objectives of this study were to investigate the relationship between dry matter intake (DMI) and urinary purine derivative (PD) excretion, to develop equations to predict DMI and to determine the endogenous excretion of PD for beef and dairy cattle using a meta-analytical approach. To develop the models, 62 published studies for both dairy (45 studies) and beef cattle (17 studies) were compiled. Twenty models were tested using DMI (kg/d) and digestible DMI (dDMI, kg/d) as response variables and PD:creatinine (linear term: PD:C, and quadratic term: PD:C^2), allantoin: creatinine (linear term: ALLA:C, and quadratic term: ALLA:C^2), metabolic body weight (BW$^{0.75}$, kg), milk yield (MY, kg/d), and their combination as explanatory variables for dairy and beef (except for MY) cattle. The models developed to predict DMI for dairy cattle were validated using an independent data set from 2 research trials carried out at the University of Wisconsin (trial 1: n = 45; trial 2: n = 50). A second set of models was developed to estimate the endogenous PD excretion. In all evaluated models, the effect of PD (either as PD:C or ALLA:C) was significant, supporting our hypothesis that PD are in fact correlated with DMI. Despite the BW-independent relationship between PD and DMI, the inclusion of BW$^{0.75}$ in the models with PD:C and ALLA:C as predictors slightly decreased the values of root mean square error (RMSE) and Akaike information criterion for the models of DMI. Our models suggest that both DMI and dDMI can be equally well predicted by PD-related variables; however, predicting DMI seems more useful from a practical and experimental standpoint. The inclusion of MY into the dairy models substantially decreased RMSE and Akaike information criterion values, and further increased the precision of the equations. The model including PD:C, BW$^{0.75}$, and MY presented greater concordance correlation coefficient (0.93 and 0.63 for trials 1 and 2, respectively) and lower RMSE of prediction (1.90 and 3.35 kg/d for trials 1 and 2, respectively) when tested in the validation data set, emerging as a potentially useful estimator of nutrient intake in dairy cows. Endogenous PD excretion was estimated by the intercept of the linear regression between DMI (g/kg of BW$^{0.75}$) and PD excretion (mmol/kg of BW$^{0.75}$) for beef (0.404 mmol/kg of BW$^{0.75}$) and dairy cattle (0.651 mmol/kg of BW$^{0.75}$). Based on the very close agreement between our results for beef cattle and the literature, the linear regression appears to be an adequate method to estimate endogenous PD excretion.

Key words: allantoin, creatinine, intake, prediction, purine derivative

INTRODUCTION

Dry matter intake is the one single parameter that most strongly influences animal performance. Therefore, reliable estimation of DMI is essential not only to evaluate animal responses in experimental settings, but also to predict performance in commercial herds. A variety of methods have been developed to estimate DMI, such as the use of indigestible markers, forage disappearance, and modeling approaches (Undi et al., 2008, Molina et al., 2004). However, problems related to those methods cause large variations in the estimates (Decruyenaere et al., 2009): for instance, incomplete fecal recovery of markers or the inability of model equations to account for the effect of sward structure on pasture intake. In fact, the wide variation among and within the methods has been identified as the primary limitation of the currently available approaches to estimate DMI (Decruyenaere et al., 2009).

Our alternative approach focuses on measuring a variable that represents a consequence of DMI variation, rather than trying to account for the causes of

Received March 21, 2017.
Accepted July 7, 2017.
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such variation. Microbial protein yield is a rumen variable that is affected by differences in DMI (Baldwin and Denham, 1979; Clark et al., 1992; Gomes et al., 1994). Although microbial protein yield, per se, is hard to measure directly, the excretion of purine derivatives (**PD**) in the urine can be used as a proxy for that variable (Valadares et al., 1999). Purine derivatives are the product of nucleic acid digestion, and because the vast majority of the nucleic acid reaching the intestine of a ruminant animal originates from ruminal microbes, a relationship is present between the amount of purines and microbial flow out of the rumen (Chen and Gomes, 1992; Fujihara and Shem, 2011). Indeed, a significant number of studies have used PD to estimate microbial CP flow from the rumen (Chen et al., 1995; Chizzotti et al., 2008; Pina et al., 2009).

Such correlation has also been used in studies to assess PD excretion in the urine as a function of the digestible organic matter intake (**dOMI**) to evaluate microbial protein yield, confirming the relationship between the 2 variables (George et al., 2006; Singh et al., 2007; Seresinhe and Pathirana, 2008). Interestingly, few studies have inverted the focus of the assessment and used PD excretion to assess dOMI (Nsahlai et al., 2000; Cetinkaya et al., 2006; George et al., 2007).

Unfortunately, total daily excretion of PD is not easily measured because it requires total collection of urine. To overcome this problem, Chen et al. (2004) developed a variable called **PDCindex** that adjusts for daily urinary volume and differences in animal size. The PDCindex is calculated by the sum of urinary PD (allantoin and uric acid) divided by the urinary creatinine and multiplied by the metabolic BW ($BW^{0.75}$, kg). This approach allows for 2 important corrections. The first is the use of creatinine to adjust for different urinary volumes, once daily creatinine excretion has been estimated to be a constant function of metabolic body mass (Vagnoni et al., 1997), and therefore can be used as a marker for urinary volume. The second is the use of the metabolic BW to correct for different animal size. As a ratio, PD:creatinine can be calculated using the concentration (mmol/L) or the total output (mmol/d) of those metabolites. Therefore, the main advantage of this method is that it only requires urine spot samples, rather than total collection. As observed by Chen et al. (2004), a strong correlation is present between PD excretion (mmol/d) and PDCindex.

Given the importance of DMI estimations and the limitations of current methods, the objective of this work was to investigate the relationship between DMI and PD to develop equations to predict DMI, and to determine the endogenous fraction of PD for beef and dairy cattle using a meta-analytical approach. Our hypothesis was that PD excretion is correlated with DMI and therefore variables related to PD (PDCindex; ratio between PD and creatinine, **PD:C**; and ratio between allantoin and creatinine, **ALLA:C**) can be used as predictors to estimate DMI.

MATERIALS AND METHODS

Database

To investigate the relationship between PD and DMI, 3 databases were reviewed: Web of Science (https://www.webofknowledge.com), Scielo (http://scielo.org/php/index.php), and Scopus (https://www.scopus.com/home.uri). Combinations of the following search terms were used: purine derivatives, allantoin, uric acid, creatinine, DMI, intake, urine, urinary excretion, PD, PD:C, and PDCindex. To be included in the data set, the paper must have reported urinary PD and creatinine (mmol/d or m*M*), DMI, BW, and DM digestibility, including their respective standard errors of the means or coefficient of variation. In addition, only studies that reported directly measured DMI were selected, considering that the main goal of the current study was to investigate the relationship between DMI and PD.

Sixty-two studies were included in the analysis, 45 with dairy cattle, comparing a total of 184 treatments means from 3,726 dairy cows, and 17 with beef cattle, comparing 59 treatments means from 809 beef animals (Appendix Table A1). In the dairy cattle data set, 1 study used dry cows (Rotta et al., 2015). Thus, we excluded this study from the data set used to estimate the endogenous fraction for lactating dairy cows. However, this study was included in the data set to predict DMI for dairy cows using PD as predictor variables.

The descriptive statistics for the dairy and beef data set is presented in Tables 1 and 2, respectively.

Model Development

Twenty models were tested using DMI (kg/d) and digestible DMI (**dDMI**, kg/d) as response variable and PDCindex, PD:C, ALLA:C, $BW^{0.75}$ (kg), milk yield (**MY**; kg/d), and their combination as explanatory variables for beef and dairy cattle (Table 3). In papers where the ratios of PD to creatinine (PDCindex, PD:C, and ALLA:C) were not reported, we calculated these variables using the reported values of allantoin, uric acid, creatinine, and BW. Dietary CP, NDF, and DIM were tested in all models, but were not significant ($P > 0.05$) in any model; therefore, we did not include those variables in the models presented in this study.

A second set of models was then developed to estimate the PD endogenous excretion. The main goal of estimating the endogenous fraction was to verify the