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Prediction of portal and hepatic blood flow from intake level data in cattle

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ABSTRACT

Interest is growing in developing integrated postabsorptive metabolism models for dairy cattle. An integral part of linking a multi-organ postabsorptive model is the prediction of nutrient fluxes between organs, and thus blood flow. The purpose of this paper was to use a multivariate meta-analysis approach to model portal blood flow (PORBF) and hepatic venous blood flow (HEPBF) simultaneously, with evaluation of hepatic arterial blood flow (ARTBF; ARTBF = HEPBF – PORBF) and PORBF/HEPBF (%) as calculated values. The database used to develop equations consisted of 296 individual animal observations (lactating and dry dairy cows and beef cattle) and 55 treatments from 17 studies, and a separate evaluation database consisted of 34 treatment means (lactating dairy cows and beef cattle) from 9 studies obtained from the literature. Both databases had information on dry matter intake (DMI), metabolizable energy intake (MEI), body weight, and a basic description of the diet including crude protein intake and forage proportion of the diet (FP; %). Blood flow (L/h or L/kg of $BW^{0.75}$/h) and either DMI or MEI (g or MJ/d or g or MJ/kg of $BW^{0.75}$/d) were examined with linear and quadratic fits. Equations were developed using cow within experiment and experiment as random effects, and blood flow location as a repeated effect. Upon evaluation with the evaluation database, equations based on DMI typically resulted in lower root mean square prediction errors, expressed as a % of the observed mean (rMSPE%) and higher concordance correlation coefficient (CCC) values than equations based on MEI. Quadratic equation terms were frequently nonsignificant, and the quadratic equations did not outperform their linear counterparts. The best performing blood flow equations were PORBF (L/h) = 202 (±45.6) + 83.6 (±3.11) × DMI (kg/d) and HEPBF (L/h) = 186 (±45.4) + 103.8 (±3.10) × DMI (kg/d), with rMSPE% values of 17.5 and 16.6 and CCC values of 0.93 and 0.94, respectively. The residuals (predicted – observed) for PORBF/HEPBF were significantly related to the forage % of the diet, and thus equations for PORBF and HEPBF based on forage and concentrate DMI were developed: PORBF (L/h) = 210 (±51.0) + 82.9 (±6.43) × forage (kg of DM/d) + 82.9 (±6.04) × concentrate (kg of DM/d), and HEPBF (L/h) = 184 (±50.6) + 92.6 (±6.28) × forage (kg of DM/d) + 114.2 (±5.88) × concentrate (kg of DM/d), where rMSPE% values were 17.5 and 17.6 and CCC values were 0.93 and 0.94, respectively. Division of DMI into forage and concentrate fractions improved the joint Bayesian information criterion value for PORBF and HEPBF (Bayesian information criterion = 6,512 vs. 7,303), as well as slightly improved the rMSPE and CCC for ARTBF and PORBF/HEPBF. This was despite minimal changes in PORBF and HEPBF predictions. Developed equations predicted blood flow well and can easily be used within a postabsorptive model of nutrient metabolism. Results also suggest different sensitivity of PORBF and HEPBF to the composition of DMI, and accounting for this difference resulted in improved ARTBF predictions.

Key words: blood flow, portal, hepatic, cattle, meta-analysis, multivariate

INTRODUCTION

The ability of current feed ration systems to predict the effects of MP supply on milk protein production and nitrogen excretion to the environment by dairy cattle is limited by an oversimplified representation of postabsorptive metabolism (Lapierre et al., 2006). Given the variability in postabsorptive metabolism, there is interest in developing integrated postabsorptive models of metabolism (portal-drained viscera, liver, mammary gland, and other organs or tissues) to replace current empirical feeding systems for cattle. Integration of such

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organ-based models requires prediction of nutrient flow between organs, including prediction of hepatic arterial (**ARTBF**), portal venous (**PORBF**) and hepatic venous (**HEPBF**) blood flows (**BF**). Across the liver, the relative contribution of ARTBF and PORBF can have a significant effect on nutrient fluxes through the organ (e.g., Barnes et al., 1986), warranting reliable prediction of these BF. Nutrient concentration in PORBF is modified by the net absorption of nutrients following digestion of feeds (or the net utilization of nutrients from arterial blood), whereas ARTBF nutrient concentration is mainly the result of the residual balance between nutrient absorption, utilization, endogenous synthesis, and mobilization from body tissues. Several attempts to model ARTBF, PORBF, and HEPBF in ruminants are present in the literature, but (1) were conducted on sheep (e.g., Vernet et al., 2009), (2) use older meta-analysis techniques that exclude random effects (e.g., Lescoat et al., 1996), or (3) examined only 1 of the 3 BF of interest (e.g., Huntington, 1984; Bermingham et al., 2008). Species differences in BF (e.g., between cattle and sheep) have already been observed (Vernet et al., 2005; Bermingham et al., 2008), indicating that cross-species application of BF equations may be inappropriate. Equations developed using older meta-analysis techniques may inherently contain prediction errors (St-Pierre, 2001; Sauvant et al., 2008). A fully integrated postabsorptive model for cattle would require all 3 BF to be estimated simultaneously. Therefore, a multivariate meta-analysis approach, simultaneously fitting equations for ARTBF, PORBF, and HEPBF, while accounting for the interrelationship between BF, is warranted.

The purpose of this study was therefore (1) to investigate the simultaneous prediction of ARTBF, HEPBF, and PORBF for cattle via a multivariate meta-analysis on published studies, considering DMI and metabolizable energy intake (**MEI**) as driving variables, and (2) to compare these predictions to available extant prediction equations on an evaluation database in order to identify the most appropriate prediction equations for use in future cattle metabolism models.

MATERIALS AND METHODS

Developmental Database

The database used for equation development is summarized in Table 1. It consisted of 17 studies with 296 individual animal means and 55 treatment means. Published experiments included Reynolds et al. (1991, 1992a,b, 1993, 1994a,b, 1995a,b, 1998, 1999, 2001, 2003a,b), Caton et al. (2001), Hanigan et al. (2004), Maltby et al. (2005), and Røjen et al. (2011). Experiments covered both lactating and dry dairy cows and growing beef cattle (steers and heifers). Method of BF measurement was downstream dilution of para-aminohippuric acid (Katz and Bergman, 1969) for all studies. Within studies, BF results were means of (between) 5 to 12 hourly measurements. All reported BF values are on a whole blood basis. Criteria for inclusion in the developmental database included availability of individual animal data and provision of information on both PORBF and HEPBF, DMI, MEI, BW, and forage % (**FP**) in the diet. Within study, any treatments that were not nutritional were removed to minimize nonnutritional variation in the database.

Within the database, the average SD within treatment across the database (indicator of within treatment animal variability) was 135 L/h, 210 L/h, 177 L/h, and 0.852 kg/d for ARTBF, PORBF, HEPBF, and DMI, respectively, and the average SD of treatment means (indicator of variation across treatment means) was 152 L/h, 548 L/h, 673 L/h, and 6.35 kg/d for ARTBF, PORBF, HEPBF, and DMI, respectively. Preliminary analysis (not shown) revealed that within-treatment BF variation was significantly related to within-treatment DMI variation ($P < 0.01$).

Evaluation Database

The database used for equation evaluation is summarized in Table 2. It consisted of 9 studies with 34 treatment means extracted from the published literature (Wieghart et al., 1986; Eisemann and Nienaber, 1990; Huntington et al., 1990; Guerino et al., 1991; Reynolds and Tyrrell, 1991; Casse et al., 1994; Eisemann and Huntington, 1994; Whitt et al., 1996; Alio et al., 2000) and included both lactating dairy cows and beef cattle. Method of BF measurement for all studies was downstream dilution of para-aminohippuric acid (Katz and Bergman, 1969). Similar to the developmental database, all reported BF values are for whole blood. Criteria for inclusion in the database included published studies with provision of information on PORBF, HEPBF, DMI, MEI, BW, and FP. Having MEI and simultaneous reporting of PORBF and HEPBF as inclusion criteria for the evaluation database limited the number of potential studies that could be included, but ensured an equal comparison between DMI and MEI, and PORBF and HEPBF based equations. Similar to the developmental database, within study, any treatments that were not nutritional were removed to minimize nonnutritional variation in the database.

The observed PORBF and HEPBF versus DMI relationship for both the developmental and evaluation databases are presented in Figure 1 and the distribution of FP across DMI in Figure 2.

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