Late Gestational Undernutrition Alters Plasma IGF-1 Concentration During Subsequent Lactation in Ewe

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Summary

The objective of this study was to investigate the effects of undernutrition during late gestation on plasma concentration of insulin-like growth factor (IGF1), leptin, insulin and glucose in pregnant and lactating ewes. Ten twin-bearing shropshire ewes were fed either adequately (AN; 100% energy and protein requirements) or restrictedly (RN; about 60% of energy and protein requirements) fed during the last six weeks of gestation. Ewe's blood samples were taken at 50, 28 and 10 days *pre-partum* as well as at lambing and 7, 17 and 35 days *post-partum*. At lambing plasma glucose concentrations sharply increased in both groups and it was significantly lower in RN ewes in comparison with AN ewes. Plasma concentrations of insulin and leptin were not affected by late gestational undernutrition. Plasma IGF1 concentrations in RN ewes (78 ±8 ng/ml) was significantly lower ($P<0.05$) than that in AN ewes (110 ±8 ng/ml). Plasma IGF1 decreased in RN ewes during late gestation and then increased sharply at lambing and during first month of lactation. In contrast IGF1 concentration was relatively constant both *pre* and *postnataly* in AN ewes. IGF1 values in restricted fed ewes were significantly lower than values in adequately fed ewes during gestation. Surprisingly IGF1 plasma in RN ewes was significantly lower at 35 days (110 vs. 164 ng/ml) *post-partum* in comparison with those in AN ewes. In conclusion, results showed late gestational undernutrion causes a decrease in plasma glucose and IGF1 at parturition as well as during late gestation. In addition, late gestational undernutrition seems to have longer term effect on plasma IGF1 even when ewes are adequately fed during lactation.

Key words

undernutrition, gestation, hormones, sheep

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Aim

Nutrition during late gestation is critical for the survival of new born lamb, colostrums and milk production in subsequent lactation (Banchero, et al., 2004). In well fed ruminant, there is flexibility during late gestation and early lactation (transition period) in which several endocrine hormones and metabolites concentrations coordinate together as pregnant animal progress from gestation to lactation. For example, plasma glucose and insulin increase dramatically around parturition and remain almost constant during prepartum and postpartum (Banchero et al., 2006; Kunz et al., 1985). Growth hormone and insulin-like growth factor (IGF1) increases (Banchero, et al. 2006). Plasma leptin increases during pregnancy and depresses during lactation (Bonnet et al., 2005). However, it is not clear whether this coordination in plasma hormones and metabolites during transition period is affected by late gestation moderate undernutrition. Therefore the aim of this study was to investigate the effect of late gestational undernutrition on blood concentrations of IGF1, leptin, insulin and glucose at parturition and during early lactation in ewe.

Material and methods

All experimental procedures complied with the guidelines of and were approved by the National Committee on Animal Experimentation, Denmark. Ten twin-pregnant shropeshire multipauruos ewes were fed either adequately (AN; 100% energy and protein requirements) or restrictedly (RN; about 60% of energy and protein requirements) according to National Research Council (NRC, 1985) during the last six weeks of gestation. The RN ewes were fed only hay silage (58 % DM, 10 MJ ME per kg DM, 8.2 % crude protein (CP), 41.9 % NDF, 9.2 % ash and 1.6 % fat) whereas the AN ewes received hay silage supplemented with barley (88.7 % DM, 10.4 % CP, 2.2 % ash and 2.3 % fat) and protein supplement (89.5 % DM, 45.4 % CP, 5.1 % ash and 5.7 % fat). After parturition, all ewes were fed *ad libitum* with hay silage plus 1000 g barley and 200 g of above mentioned protein supplement. Ewe's blood samples were taken at 9.00 a.m. on 50, 28 and 10 day *pre-partum* as well as at lambing, 7, 17 and 35 days *post-partum*. All samples were taken by vein puncture of the jugular vein, and blood was collected in 10 ml heparin-flourine vacuum tube (Vacuntainer™, Becton Dickinson Vacuntainer System Europe, Meylan Cradex, France) and 10 ml EDTA vacuum tube (BD Vacuntainer System, Preanalytical Solution Deliver Industrial Estate Plymouth PL6 7 BP, UK). Blood samples were immediately cooled on ice and then centrifuged at 3000 r.p.m. for 15 min at 4 °C within 30 min after collection. Plasma samples were transferred to polystyrene tubes (Hounissen, Rossikov, Denmark) and frozen at -20 °C pending analysis. Plasma concentrations of glucose were analyzed by commercially available spectrophotometric kit (17-25 Infinity™, Sigma Diagnostic® Inc, P. O. Box 14508, St. Louis, MO 63178, USA). Plasma insulin concentration was determined by a sandwich-type time-resolved fluoroimmunoassay (DELFIA) as described by (Ingvartsen et al., 1999). Plasma samples for leptin were freeze dried and analyzed at the University of Western Australia, Perth. Leptin analyses were performed in duplicate by a double-antibody radioimmunoassay using ovine leptin raised against bovine leptin as described by (Blache et al., 2000). The limit of detection was 0.07 ng/ml. Plasma IGF-I concentration was determined by double-antibody RIA with human recombinant IGF-I and antihuman IGF-I antiserum according to (Breier et al., 1991). Normality of residuals was tested using Shapiro-Wilks test. Repeated measurements of plasma hormones and metabolites were analyzed using the following linear mixed model with the MIXED procedure in SAS version V8.2.:

$$Y_{ij} = \mu + \alpha_i + \beta_j + (\alpha\beta)_{ij} + e_{ij},$$

where μ was the population mean, α_i was the fixed effect of late gestation maternal nutrition, β_j was the fixed effects of sample time and $(\alpha\beta)_{ij}$ was the interactions between fixed effects. e_{ijk} was the residual error (Littell et al., 2000). Samples within each ewe were declared as repeated If any of the systematic interaction effects did not reach significance (P>0.05), it was eliminated from the model. Based on likelihood ratio test, the covariance structure of the repeated measurements was modeled as compound symmetry (CS), auto-regressive order 1 (AR1) or unstructured (UN) (Littell et al., 2000).

Results and discussion

Ewes body weights and their body condition score (BCS) are shown in Figure 1. At the beginning of the experiment, means of ewe's weight were 90 and 89 kg for AN and RN group respectively. Late gestational nutrient restriction reduced body weight of RN ewes about 7 kg whereas no decrease was observed in AN

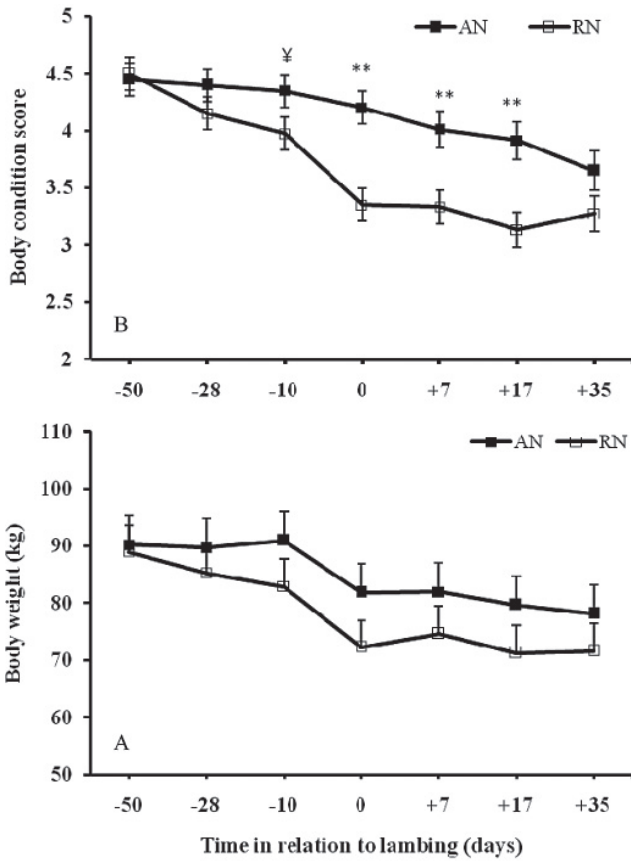

Figure 1. Body weight (A) and body condition score (B) of ewes fed either 60% (RN; □) or 100% (AN; ■) of their energy and protein requirements during the last six weeks of gestation. ¥ P< 0.1, * P< 0.05, ** P< 0.01.

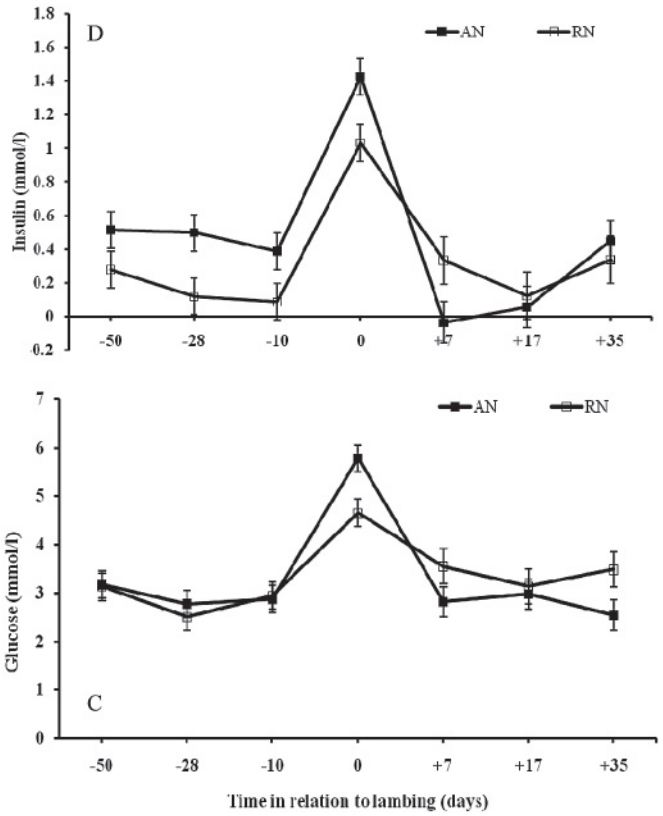

Figure 2. Plasma glucose (C) and insulin concentrations (D) of ewes fed either 60% (RN; □) or 100% (AN; ■) of their energy and protein requirements during the last six weeks of gestation. ¥ P< 0.1, * P< 0.05, ** P< 0.01.

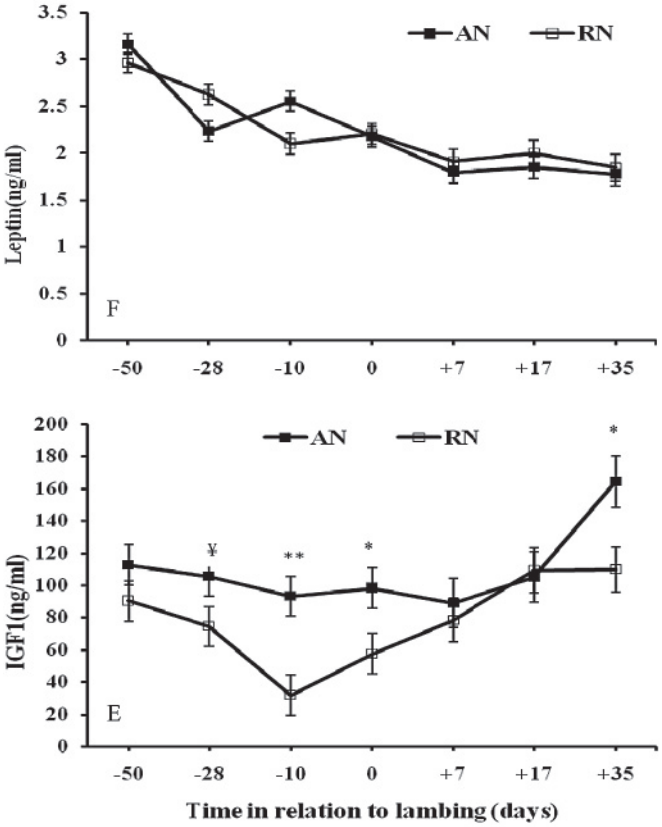

Figure 3. Plasma Insulin-like growth factor (IGF1) (E) and leptin (F) concentrations of ewes fed either 60% (RN; □) or 100% (AN; ■) of their energy and protein requirements during the last six weeks of gestation. ¥ *P*< 0.1, * *P*< 0.05, ** *P*< 0.01.

ewes during the last two months of gestation. After parturition, means body weight was 82 and 72 kg and thereafter ewe's weights were constant. Body condition score for both groups was 4.5 at the commencement of the experiment. Nutrient restriction significantly reduced BCS in RN in comparison with AN ewes. At parturition day, BCS in RN ewes (3.3) was significantly ($P<0.05$) lower than that in AN ewes (4.2). Plasma concentration of glucose and insulin are shown in Figure 2. Result showed that both glucose and insulin dramatically increased around parturition and remained constant in *pre-partum* and *post-partum* respectively. These results were in agreement with values reported in similar study in which ewes were fed adequately or restricted during late gestation (Banchero et al., 2006). In present study the RN ewes had significantly lower ($P<0.05$) concentration of glucose than AN ewes at lambing in spite of having the same values for insulin.

Plasma concentration of leptin and IGF1 are shown in Figure 3. No significant differences were found between two groups in respect to leptin concentration in plasma. Plasma leptin decreased during gestation and its concentration during lactation was significantly ($P<0.05$) lower than its concentration during gestation. In both groups, leptin concentration gradually declined throughout late gestation and lactation. Leptin values in this experiments were higher than those reported previously for sheep (Thomas et al., 2001) and were in agreement with other reports (Bonnet et al., 2005; Banchero et al., 2006). Regardless to the time of blood sampling, plasma IGF1 concentration in RN ewes (78±8 ng/ml) was significantly lower ($P<0.05$) than that in AN ewes (110±8 ng/ml). In addition, IGF1 plasma in RN ewes was significantly ($P<0.05$) lower at 28 (74 vs. 106 ng/ml), 10 (32 vs. 93 ng/ml) days *pre-partum* and 35 days (110 vs. 164 ng/ml), *post-partum* in comparison with those in AN ewes. IGF1 concentration was relatively constant both *pre* and *post-nataly* in AN ewes whereas its plasma concentration decreased in RN ewes during late gestation and then increased ($P<0.05$) sharply at parturition and during first month of lactation. IGF1 values in AN ewes were similar to values of adequate nourished ewes (Banchero et al., 2006). IGF1 values in restricted fed ewes were lower than values in adequately fed ewes during gestation. Surprisingly IGF1 plasma concentration remained low even when ewes were adequately nourished during lactation period.

Conclusions

In conclusion, results showed that there is flexibility and coordination between several endocrine hormones and metabolites concentrations during late gestation and early lactation (transition period). Plasma glucose and insulin increase dramatically around parturition and remain almost constant during prepar-

tum and postpartum. Plasma leptin decreases during both gestation and lactation period. Insulin-like growth factor remains constant during transition period. Late gestational undernutrion causes a disorder in hormones coordination during transition period which is reflected in plasma glucose and IGF1 at parturition as well as during late gestation. In addition, late gestational undernutrition has longer term effect on plasma IGF1 even during lactation when the ewes are adequately fed. This finding may relate to less colostrums and milk production in lactating ewes with late gestational undernourished background.

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