Immune Activation Modifies Hepatic Energy Metabolism in Early-Lactation Cows

The liver plays a key role in regulating nutrient partitioning during the early lactation period in dairy cows. The aim of this study was to determine hepatic mitochondrial function in dairy cows subjected to systemic immune activation. Sixteen multiparous Holstein cows (body weight 639 ± 68 kg; body condition score 3.0 ± 1.4) at 15 ± 8 days postpartum were intravenously infused with lipopolysaccharides (LPS) (62.5 ng/kg body weight; n = 8, LPS) or sterile saline as a control (n = 8, CTRL). Cows were offered a total mixed ration [18% crude protein and 36% neutral detergent fiber on a dry matter basis] and were milked twice daily. Cows administered LPS had a 36% reduction in dry matter intake and 13% reduction in milk yield; CTRL cows were pair-fed to ensure comparable intake between treatments. Activation of the immune response was evidenced by elevated rectal temperature (peak mean of 40.3°C at 3 h post-infusion), along with increased heart rate (103 beats/min) and respiratory rate (70 breaths/min). Liver biopsies were collected 24 hours after infusion and mitochondrial function was assessed measuring oxygen consumption rates using complex I (glutamate/malate) and complex II (succinate) substrates, followed by the addition of oligomycin, uncoupler carbonyl cyanide 4-(trifluoromethoxy)phenylhydrazone (FCCP), and antimycin A plus rotenone using high resolution respirometry. No changes were observed for complex I-driven respiration. However, higher State 3 (26.9 vs. 17.2 ± 3.2 pmolO2/min/mg, $P < 0.05$) and oligomycin-sensitive respiration -represented ATP-linked respiration- were observed for LPS cows (5.4 vs. 2.3 ± 0.9 pmolO2/min/mg, $P < 0.05$) when complex II was evaluated. Additionally, no differences in energy corrected milk were observed between treatments, however, milk urea nitrogen concentrations were elevated in LPS cows (17.5 vs. 14.1 ± 0.5 mg/dL, $P < 0.05$). Collectively, these results indicate that immune activation increases complex II–driven ATP synthesis in the liver of early-lactation dairy cows, potentially reflecting enhanced anaplerotic flux to support gluconeogenesis and/or protein synthesis during inflammation.

immunometabolism, inflammation, dairy cattle

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