Pegbovigrastim affected gene expression in neutrophils of transition cows indicating increased neutrophil function

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Introduction

Treatment of transition cows with granulocyte colony stimulating factor (G-CSF) has been shown to increase neutrophil count and function. It was hypothesized that prepartum under-nutrition might reduce the effect of a commercial recombinant bovine G-CSF product (pegbovigrastim; Imrestor, Elanco). Hence this study was undertaken to test the effect of under-nutrition and pegbovigrastim treatment on gene expression in neutrophils.

Materials and Methods

Pasture-fed cows (n=99) in New Zealand were blocked by calving date and BCS and randomly assigned in a 2×2 factorial design to be fed prepartum to exceed energy requirements or restricted to 85% of energy requirements. Half of the animals in each group were injected with the labelled dose of pegbovigrastim or saline at approximately 7 d before expected calving and again on the day of calving. Blood samples were collected 7 d pre-calving (D -7) and blood, uterine fluid, and milk samples were obtained on D4 and D7 after calving. Gene expression analysis was performed for 21 genes, representing key aspects of inflammation, and neutrophil activation, migration, phagocytosis, oxidative burst, and apoptosis using NanoString.

Results

Effects of time and pegbovigrastim treatment were observed, but under-feeding did not affect gene expression. On average, cows showed higher expression of almost all selected genes at D4 compared to D -7, including genes for migration and inflammation markers (e.g., L-selectin, ICAM1, and TLR 2; $P < 0.05$) indicating an ongoing neutrophil response to the hormonal and metabolic stresses of the parturition and postpartum infections. Pegbovigrastim treatment enhanced the effect by further increasing expression of ICAM1 and TLR2 ($P < 0.05$), suggesting increased neutrophil efficiency. In uterine fluid and to a lesser degree in milk, pegbovigrastim lowered expression of migration markers and increased expression of genes for other neutrophil functions, including myeloperoxidase, FAS, and caspase 2 (the latter 2 reflecting apoptosis or cell survival) ($P < 0.05$) potentially increasing neutrophil effectiveness.

Significance

Pegbovigrastim treatment resulted in significant increases in the expression of genes involved in inflammation, phagocytosis, respiratory burst, degranulation, and apoptosis/survival of neutrophils in blood, uterine fluid and milk, and also migration of blood neutrophils.