

Upregulation of Proinflammatory Cytokine Production in Response to Bacterial Pathogen-Associated Molecular Patterns in Dogs with Diabetes Mellitus Undergoing Insulin Therapy

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Abstract

Background:

Metabolic alterations associated with diabetes mellitus alter innate immunity. Dogs often develop infectious or inflammatory complications related to diabetes mellitus, yet little is known about the effects of diabetes mellitus on the immune system in this species.

Methods:

Prospective evaluation in dogs with poorly regulated spontaneous type 1 diabetes mellitus (T1DM). *In vitro* leukocyte cytokine response to lipopolysaccharide (LPS), lipoteichoic acid (LTA), and peptidoglycan (PG) was compared between dogs with T1DM and healthy dogs. Additionally, the effect of acute *in vitro* glucose exposure on leukocyte tumor necrosis factor (TNF) production from healthy dogs was measured.

Results:

Leukocytes from dogs with T1DM had significantly greater TNF production after LTA and PG stimulation compared with leukocytes from healthy dogs. Leukocyte interleukin (IL)-6 production was greater after stimulation with LPS, LTA, PG, and phosphate-buffered saline in the T1DM group. No such difference was noted when evaluating IL-10 production between groups regardless of stimulant. Dogs with T1DM had significantly greater IL-6 to IL-10 production ratios than healthy dogs. Acute exposure to dextrose did not augment cytokine production from healthy canine leukocytes.

Conclusions:

Dogs with T1DM have altered innate immunity characterized by upregulation of proinflammatory cytokine production without a concurrent change in anti-inflammatory cytokine production. This may be one explanation for the common infectious and inflammatory complications associated with T1DM in dogs.

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Abbreviations: (IL) interleukin, (LPS) lipopolysaccharide, (LTA) lipoteichoic acid, (PAMP) pathogen-associated molecular pattern, (PBMC) peripheral blood mononuclear cell, (PBS) phosphate-buffered saline, (PG) peptidoglycan, (RPMI) Roswell Park Memorial Institute, (T1DM) type 1 diabetes mellitus, (TNF) tumor necrosis factor

Keywords: immunology, interleukin, lipopolysaccharide, lipoteichoic acid, tumor necrosis factor

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