

EVALUATION OF THE ANTIENDOTOXIN EFFECTS OF POLYMYXIN B IN A FELINE MODEL OF ENDOTOXEMIA

Claire R. Sharp

Dr. Carol Reinero, Thesis Supervisor

ABSTRACT

Introduction: Directed, effective therapies for feline sepsis are needed to reduce the high morbidity and mortality associated with this disease.

Materials and Methods: We investigated the anti-endotoxin effects of PMB in a blinded, placebo controlled fashion, both *ex vivo* in a feline whole blood culture system and *in vivo*, using a low-dose endotoxin infusion in cats (2ug/kg/hr IV x 4 hours). Serial measures of systemic inflammation, and hemodynamic stability, were compared between groups.

Results: *Ex vivo*, PMB significantly decreased LPS-induced TNF production from whole blood. *In vivo*, endotoxin infusion resulted in the development of fever, hypotension, leucopenia and increased TNF activity. Polymyxin B (1mg/kg over 30 minutes) treatment decreased peak plasma TNF activity ($p < 0.001$) and increased white blood cell count ($p = 0.019$), with no adverse effects.

Conclusions: Polymyxin B administration resulted in decreased peak plasma TNF activity and increased white blood cell count in this feline model of endotoxemia, with no adverse effects. Given the apparent safety and anti-endotoxin effects of PMB in this endotoxemia model, a carefully designed, randomized, blinded, placebo controlled clinical trial evaluating the use of PMB in naturally occurring Gram negative feline sepsis should be considered.