INFLUENCE OF INTERLEUKIN-1 ON NEUTROPHIL FUNCTION AND RESISTANCE TO *STREPTOCOCCUS SUIS* IN YOUNG PIGS

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Summary

Nonspecific immunity is usually lower in young pigs than adults. Consequently, enhancing the young pig's nonspecific immune capability may be beneficial for the health and performance of early-weaned pigs. Twenty, 9-d-old, crossbred pigs were allotted by litter and weight into two treatment groups: recombinant bovine interleukin-1β (rBoIL-1β; 5 µg/kg, intramuscularly at 9 and 10 d of age)) or control. Pigs were weaned at 10 d of age and housed in an isolation facility with ad libitum access to water and a pelleted diet formulated to meet the nutrient requirements and provide maximum growth of early-weaned pigs. Blood samples were obtained on 9, 12, 15, and 18 d of age for determination of several neutrophil function assays including: bactericidal activity, antibody-dependent cellular cytotoxicity (ADCC), and superoxide anion production. Pigs were challenged with *S. suis* (serotype 2) at 18 d of age. Neutrophil-mediated ADCC was increased at 12, 15, and 18 d of age in pigs treated with rBoIL-1β. Two days postweaning, neutrophil-mediated lysis of *Staphylococcus aureus* was lower in control pigs when compared to rBoIL-1β-treated pigs (6.6 vs 13.3%). Superoxide anion production was not influenced by rBoIL-1β treatment. Clinical signs of *S. suis* infection were less severe in pigs administered rBoIL-1β. These data suggest that rBoIL-1β increases neutrophil function and resistance to *S. suis* in early-weaned pigs.

(Key Words: Early Weaning, Immunity, Immune Enhancement.)

Introduction

Newborn animals lack a fully competent immune system. This situation is particularly relevant in pigs for several reasons. For example, it has been repeatedly shown that young pigs have low or absent nonspecific immune responses. This finding is usually illustrated by low or absent natural killer cell activity in neonatal pigs until approximately 2 to 3 weeks of age. Additionally, neutrophil functions have been shown to be lower in neonatal pigs when compared to adult values. These observations suggest that enhancing the young pig's nonspecific immune capability may be beneficial and may allow early weaning without the extensive reliance on mass medication of the newborn.

One approach to immune enhancement is the use of cytokines. Interleukin-1 (IL-1) and interleukin-2 (IL-2) have been shown to have specific and nonspecific immuno-

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modulating functions in immunosuppressed or neonatal animals, and enhancement of nonspecific antibacterial resistance by IL-1 is well documented. Porcine IL-1α, IL-1β, and IL-2 have been cloned and expressed, but are not available in sufficient quantities for in vivo experiments. However, porcine IL-1β and bovine IL-1β have a high degree of similarity, and recombinant bovine IL-1β (rBoIL-1β) is biologically active in pigs. Therefore, the purpose of this study was to investigate the influence of rBoIL-1β on nonspecific immunity and disease resistance in young pigs.

Procedures

Twenty, 9-d-old, crossbred pigs from three litters were allotted by litter and weight into two groups: rBoIL-1β (5 µg/kg, intramuscularly, at 9 and 10 d of age) or control (equal volume of physiologic saline, intramuscularly). Pigs were weaned at 10 d of age and housed in an isolation facility in polyethylene pens (Poly Dome Pig Nursery, Litchfield, MN). Pigs had ad libitum access to water (nipple waterers) and a pelleted diet formulated to meet the nutrient requirements and provide maximum growth of early-weaned pigs. Blood samples were obtained on 9, 12, 15, and 18 d of age for determination of neutrophil bactericidal activity, antibody-dependent cellular cytotoxicity (ADCC), and superoxide anion production. Pigs were inoculated intravenously with *Streptococcus suis*, serotype 2, (3×10^9 CFU) at 18 d of age, and clinical signs were monitored and recorded daily for 7 d.

Results and Discussion

Two days after weaning, the capability of neutrophils to lyse *S. aureus* was lower ($P<.05$) in control pigs (6.6%±2.1) than in rBoIL-1β-treated pigs (13.0%±2.0). This finding suggests that IL-1 treatment prevented a weaning-induced decrease in neutrophil bactericidal activity. Although neutrophil production of superoxide anion did not differ between the two groups, neutrophil-mediated antibody-dependent cellular cytotoxicity was increased ($P<.05$) after rBoIL-1β administration. When pigs were challenged with *S. suis*, rBoIL-1β-treated pigs had a significantly lower severity of disease than the saline-injected controls (Fig. 1).

Interleukin-1 is a predominantly macrophage or monocyte-derived protein that modulates many of the responses involved in the process of host defense to infection, including neutrophil functions, such as adherence, cell migration, respiratory burst, lysosomal enzyme release, and cell surface receptor expression. Our data suggest that rBoIL-1β may selectively enhance neutrophil antimicrobial activity and increase resistance to streptococcal infection in neonatal pigs. Thus, age- or early-weaning-associated immune defects in young pigs may be improved by administration of interleukin-1.

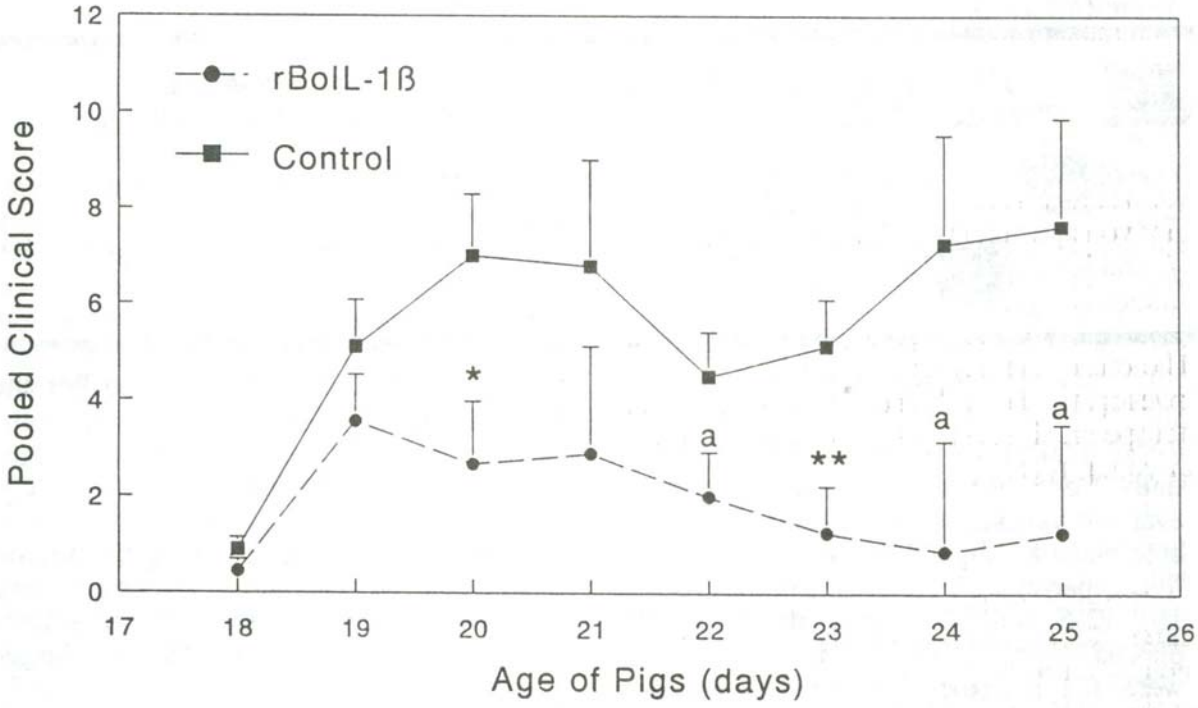

Figure 1. Pooled Clinical Signs after *S. suis* Challenge in Pigs Treated with rBoIL-1β or Saline (Control). Pigs were weaned at 10 d of age, injected intramuscularly with rBoIL-1β (5 µg/kg at 9 and 10 d of age) or physiologic saline, and inoculated intravenously with *S. suis*, serotype 2, (3×10^9 CFU) on d 18. Clinical score increases in severity of disease from 0 to 10 and includes dyspnea, lameness, depression, CNS signs, and rectal temperature. Values are means ± SEM, n=10, ^{a}P<.07, *P<.05, **P<.01