Synergistic Roles of Host Immunity and Antibiotic Treatment in Reducing Bacterial Infection in Mice

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***Abstract*:**

Background: Antibiotics and host immunity are often considered independent defenses, with antibiotics primarily reducing bacterial burden to levels manageable by immune clearance. Using a *Pseudomonas aeruginosa* wound infection model in immunocompetent (C57BL/6) and immunocompromised (NSG) mice, we hypothesized that tobramycin-mediated bacterial killing releases pathogen-associated molecular patterns (PAMPs) that activate innate immune signaling, enhance inflammatory responses, and promote leukocyte recruitment, thereby improving infection control. We further postulated that this synergistic interaction is impaired in immunocompromised hosts, leading to reduced antibiotic efficacy.

Methods: Tobramycin was administered intraperitoneally to C57BL/6 and NSG mice prior to wound challenge with PA103 (10^6 CFU/wound). Wounds were harvested 24 hours post-infection to assess bacterial burden, bioactive LPS levels, Toll-like receptor expression, pro-inflammatory cytokine production, leukocyte infiltration, and neutrophil activation. To test whether reduced PAMP availability contributed to impaired immune responses in NSG mice, a low dose of LPS was topically applied to wounds before infection. Neutrophil depletion studies using anti-Ly6G antibodies were performed to define the role of neutrophils.

Results and Conclusions: Tobramycin treatment amplified innate immune responses in immunocompetent mice, resulting in enhanced inflammatory signaling, robust neutrophil recruitment, and effective bacterial clearance. This immune amplification was absent in NSG mice but was restored by topical PAMP supplementation. Neutrophil depletion abrogated the observed synergy, identifying neutrophils as key mediators. These findings support combining antibiotics with innate immune modulators to improve infection outcomes, particularly in immunocompromised hosts.

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