Vancomycin Exposure Enhances Virulence in Stenotrophomonas maltophilia, an Emerging Nosocomial Pathogen

MARIA CARDENAS 1, BRIDGET EKLUND 1, SANJIVNI SINHA 1, NATHAN FISHER 1
1. North Dakota State University

ABSTRACT

Background. Stenotrophomonas maltophilia is an emerging, multi-drug resistant bacterium associated with a wide spectrum of life-threatening, hospital acquired infections. Attributable mortality rates can be extremely high-above 37% after adjusting for underlying conditions-and both incidence and prevalence are on the rise. However, asymptomatic colonization is also common and S. maltophilia isolates are largely avirulent in vitro. Since invasive disease often follows antibiotic therapy, we hypothesized that S. maltophilia may respond to non-lethal antibiotic stress by adopting a hyper-virulent state.

Methods. In order to test this hypothesis, we measured S. maltophilia virulence using three invertebrate assays in the presence and absence of vancomycin, one of the most commonly prescribed antibiotics preceding S. maltophilia infection. First, the ability to resist predation by Dictyostelium discoideum amoeba was used to assay interactions between S. maltophilia and phagocytic eukaryotic cells. Then, we characterized interactions between S. maltophilia and multicellular organisms with intact immune systems using the nematode Caenorhabditis elegans and juvenile Blaptica dubia roaches.

Results. In the absence of antibiotic exposure, virulence toward amoeba and nematodes varied widely among 18 genetically diverse isolates. However, all isolates were avirulent in our insect assay (lethal dose 50% >10^7 CFU). Interestingly, vancomycin exposure resulted in a striking enhancement of virulence toward amoeba, nematodes, and insects for all S. maltophilia isolates tested (n=8 representative isolates). In some cases, the minimum number of amoeba cells required to form a plaque on a lawn of S. maltophilia increased more than 1000-fold. Exposure to vancomycin also led to significant decreases in insect and nematode survival. Notably, vancomycin-induced virulence was evident in both clinical and environmental isolates of S. maltophilia but was not observed in other bacterial pathogens including Pseudomonas aeruginosa.

Conclusions. Our results indicate that vancomycin, one of the most commonly prescribed antibiotics in many hospitals, induces otherwise dormant virulence pathways that may contribute to the invasiveness and severity of disease caused by S. maltophilia.

This is a pre-print upload of the abstract, as we currently finishing experiments and refining the manuscript body. We would love feedback and suggestions, if you find the topic interesting. ^NF
VANCOMYCIN EXPOSURE ENHANCES VIRULENCE IN STENOTROPHOMONAS MALTOPHILIA, AN EMERGING NOSOCOMIAL PATHOGEN: BIOLOGICAL SCIENCES

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