The Interplay of Antibiotic Resistance and Virulence Attenuation in *Acinetobacter baumannii*: Profiling Alterations in Pathogenicity in Response to Antibiotic Pressure Over 14 Days

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ABSTRACT

**OBJECTIVES**

1. To define the relationship between the emergence of polymyxin B resistance and the pathogenicity of A. baumannii.

**METHODS**

1. *A. baumannii* strain 03-149-1 was front loaded with 1.0 and resistant to all carbapenems, but was susceptible to Polymyxin B and the non-mammalian Galleria mellonella waxworm model.
2. Isolates were taken during incubation at 0hr, 24hr, 48hr, 72hr, 96hr, 144hr, 192hr, 240hr, 288hr, and 336hr respectively.
3. Following intense polymyxin B selection pressure at 10mg/L, the isolates exposed in the Hollow Fiber Infection Model for 244hrs were resistant by the time of injection into the waxworms for the virulence assays.
4. The inocula used for the virulence assay, there were no statistically significant differences between any experimental or control groups.
5. In the virulence assay, the 0hr, 24hr, 48hr, 72hr, 96hr, 144hr, 192hr, and 192hr isolates all had significantly lowered survival rates (p<0.001 for 0hr-92hr isolates, p=0.05 144hr and 192 isolates).

**RESULTS**

1. Polymyxin B 10mg/ml exposure in the Hollow Fiber Infection Model. 2. The lowest survival rate of 0% was seen in the 48hr isolate group, while the highest survival rate of 80% was seen in the 336hr isolate group, p<0.001.
3. Comparing the in ocula used for the virulence assay, there were no statistically significant differences between any experimental or control groups.
4. In the virulence assay, the 0hr, 24hr, 48hr, 72hr, 96hr, 144hr, and 192hr isolates all had significantly lowered survival rates (p<0.001 for 0hr-92hr isolates, p=0.05 144hr and 192 isolates).
5. Survival rates of waxworms injected with the 240hr, 288hr, and 336hr isolates did not show significant results when compared to the control group, p>0.05.

**CONCLUSIONS**

1. The development of resistant *A. baumannii* emerged as more time was spent in the Hollow Fiber Infection Model due to increasing polymyxin B exposure.
2. The emergence of resistance had a significant effect on the virulence of *A. baumannii*. The increasing polymyxin B MICs counter selected for resistance, which attenuated virulence capacity.
3. Overall, these findings could play a vital role in the pharmacotherapy of patients in the ICU with persisting infection. As prolonged antibiotic regimes may be necessary treatment, there still presents the risk of an attenuated strain due to the interplay between antibiotic resistance and virulence.

**REFERENCES**

1. Emergence of colistin resistance without loss of fitness and virulence after prolonged colistin administration in a patient with extended-drug-resistant *Acinetobacter baumannii*.

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